09/446543

[Drawing]

Fig. 1

```
                              9                     18                          27                    36                          45                          54
5' GTG GGC ATG GTG GGC AAC GTC CTG CTG GTG CTG GTG ATC GCG CGG GTG CGC CGG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Val Gly Met Val Gly Asn Val Leu Leu Val Leu Val Ile Ala Arg Val Arg Arg

                             63                     72                          81                    90                          99                         108
   CTG CAC AAC GTG ACG AAC TTC CTC ATC GGC AAC CTG GCC TTG TCC GAC GTG CTC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu His Asn Val Thr Asn Phe Leu Ile Gly Asn Leu Ala Leu Ser Asp Val Leu

                            117                    126                         135                   144                         153                         162
   ATG TGC ACC GCC TGC GTG CCG CTC ACG CTG GCC TAT GCC TTC GAG CCA CGC GGC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Met Cys Thr Ala Cys Val Pro Leu Thr Leu Ala Tyr Ala Phe Glu Pro Arg Gly

                            171                    180                         189                   198                         207                         216
   TGG GTG TTC GGC GGC GGC CTG TGC CAC CTG GTC TTC TTC CTG CAG CCG GTC ACC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Trp Val Phe Gly Gly Gly Leu Cys His Leu Val Phe Phe Leu Gln Pro Val Thr

                            225                    234                         243                   252                         261                         270
   GTC TAT GTG TCG GTG TTC ACG CTC ACC ACC ATC GCA GTG GAC CGG TAC GTC GTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Val Tyr Val Ser Val Phe Thr Leu Thr Thr Ile Ala Val Asp Arg Tyr Val Val

                            279                    288                         297
   CTG GTG CAC CCG CTG AGG CGG CGC ATC 3'
   --- --- --- --- --- --- --- --- ---
   Leu Val His Pro Leu Arg Arg Arg Ile
```

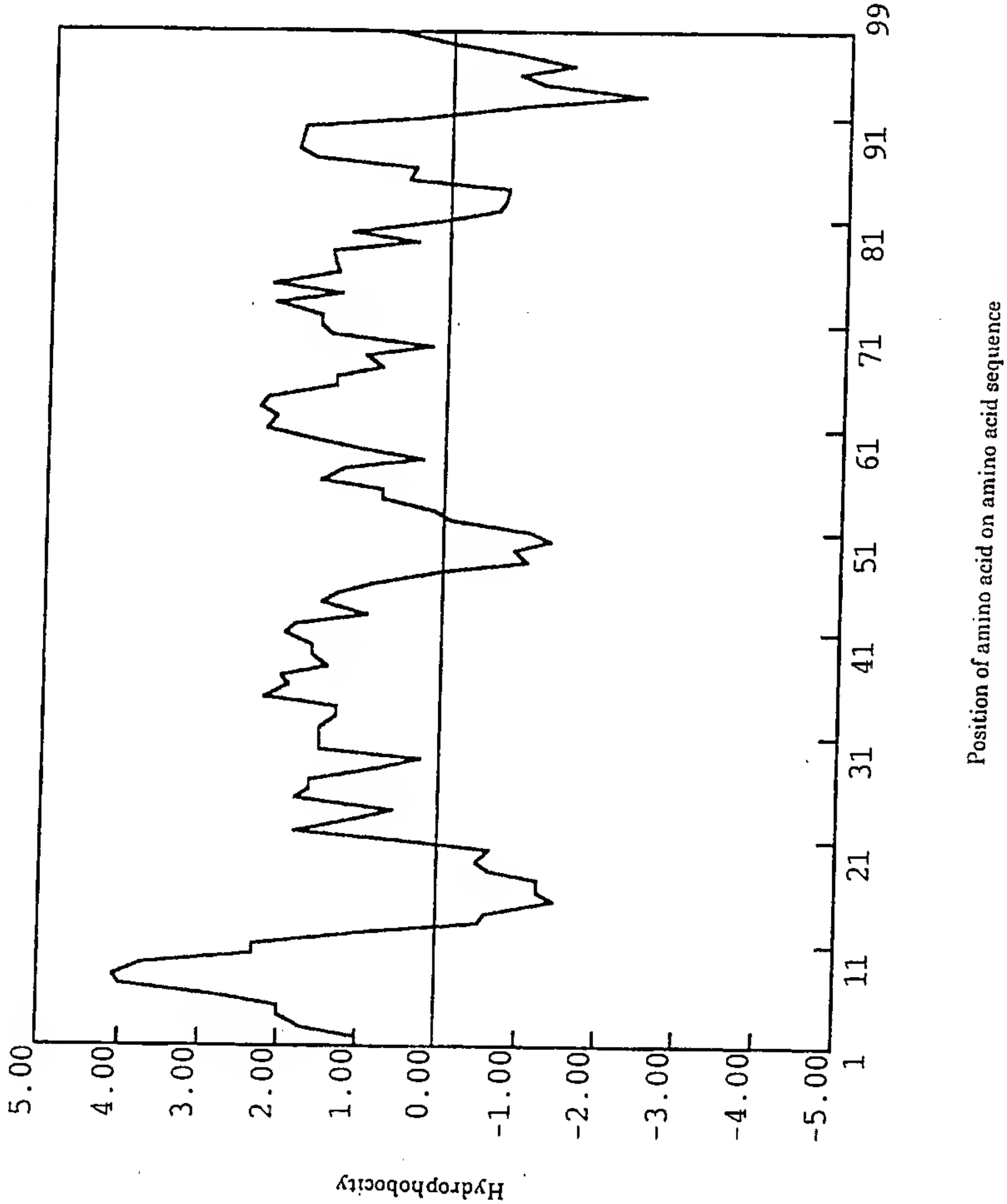
09/446543

Fig. 2

```
                9          18          27          36          45          54
5'  GGC CTG CTG CTG GTC ACC TAC CTG CTC CCT CTG CTG GTC ATC CTC CTG TCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Gly Leu Leu Leu Val Thr Tyr Leu Leu Pro Leu Leu Val Ile Leu Leu Ser Tyr

               63          72          81          90          99         108
    GTC CGG GTG TCA GTG AAG CTC CGC AAC CGC GTG GTG CCG GGC TGC GTG ACC CAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Val Arg Val Ser Val Lys Leu Arg Asn Arg Val Val Pro Gly Cys Val Thr Gln

              117         126         135         144         153         162
    AGC CAG GCC GAC TGG GAC CGC GCT CGG CGC CGG CGC ACC TTC TGC TTG CTG GTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Ser Gln Ala Asp Trp Asp Arg Ala Arg Arg Arg Arg Thr Phe Cys Leu Leu Val

              171         180         189         198
    GTG GTC GTG GTG GTG TTT GCC ATC TGC TGG TTG CCT TAC TAC 3'
    --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Val Val Val Val Val Phe Ala Ile Cys Trp Leu Pro Tyr Tyr
```

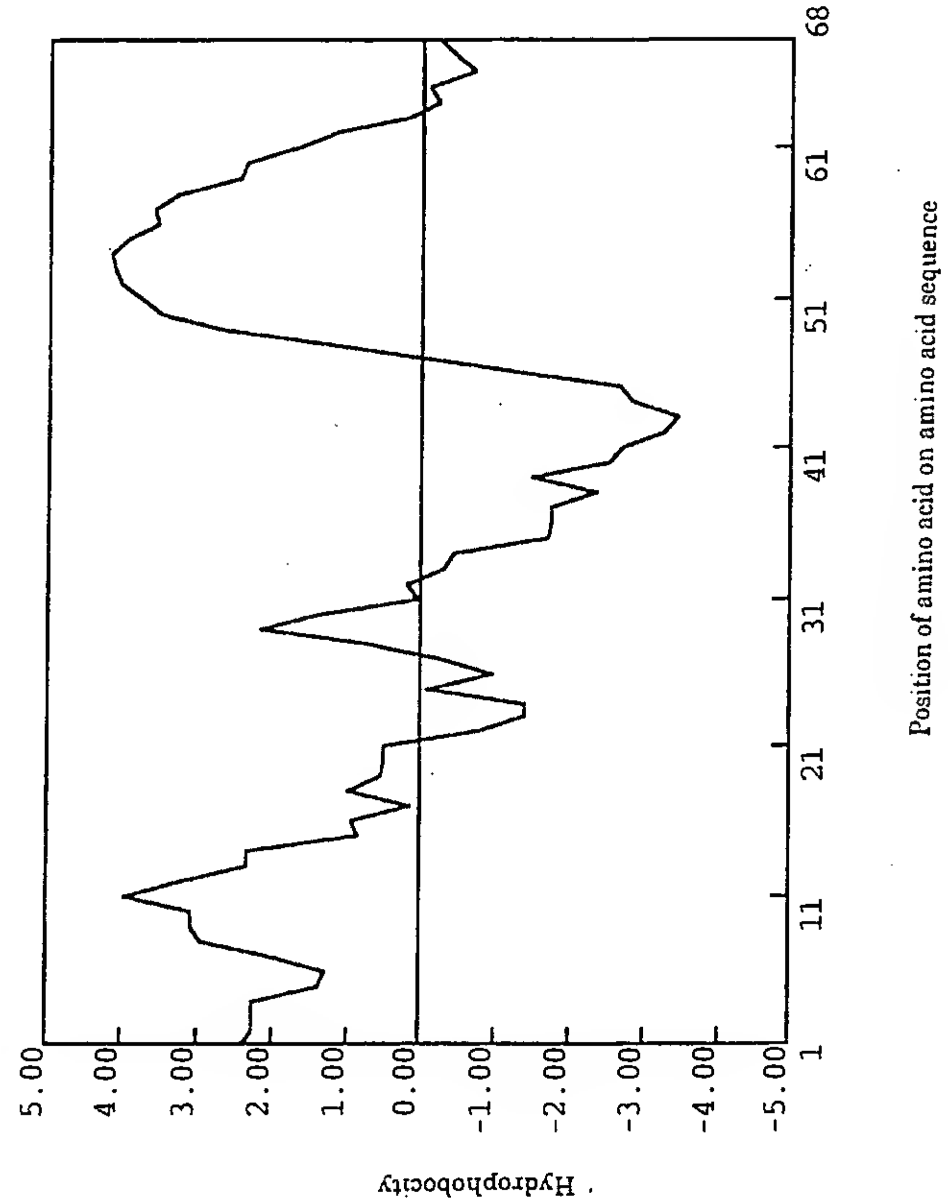
09/446543

Fig. 3



09/446543

Fig. 4



09/446543

Fig. 5

```
                         10         20         30         40         50
p19P2     1 VGMVGNVLLV LVIARVRRLH NVTNFLIGNL ALSDLLMCTA CVPLTLAYAF   50
S12863    1 LGVSGNLALI IIILKQKEMR NVTNILIVNL SFSDLLVAVM CLPFTFVYTL   50

                         60         70         80         90        100
p19P2    51 EPRGWVFGGG LCHLVFFLQP VTVYVSVFTL TTIAVDRYVV LVHPLRRRI-  100
S12863   51 MDH-WVFGET MCKLNPFVQC VSITVSIFSL VLIAVERHQL IINPRGWRPN  100

                        110        120        130        140        150
p19P2   101 ---------- ---------- ---------- ---------- ----------  150
S12863  101 NRHAYIGITV IWVLAVASSL PFVIYQILTD EPFQNVSLAA FKDKYVCFDK  150

                        160        170        180        190        200
p19P2   151 -----GLLLV TYLLPLLVIL LS-------Y VRVSVKLRNR VVPGCVTQSQ  200
S12863  151 FPSDSHRLSY TTLLLVLQYF GPLCFIFICY FKIYIRLKRR NNMMDKIRDS  200

                        210        220        230        240        250
p19P2   201 ADWDRARRRR TFCLLVVVVV VFAICWLPYY .......... ..........  250
S12863  201 KYRSSETKRI NVMLLSIVVA -FAVCWLPLT .......... ..........  250
```

09/446543

Fig. 6

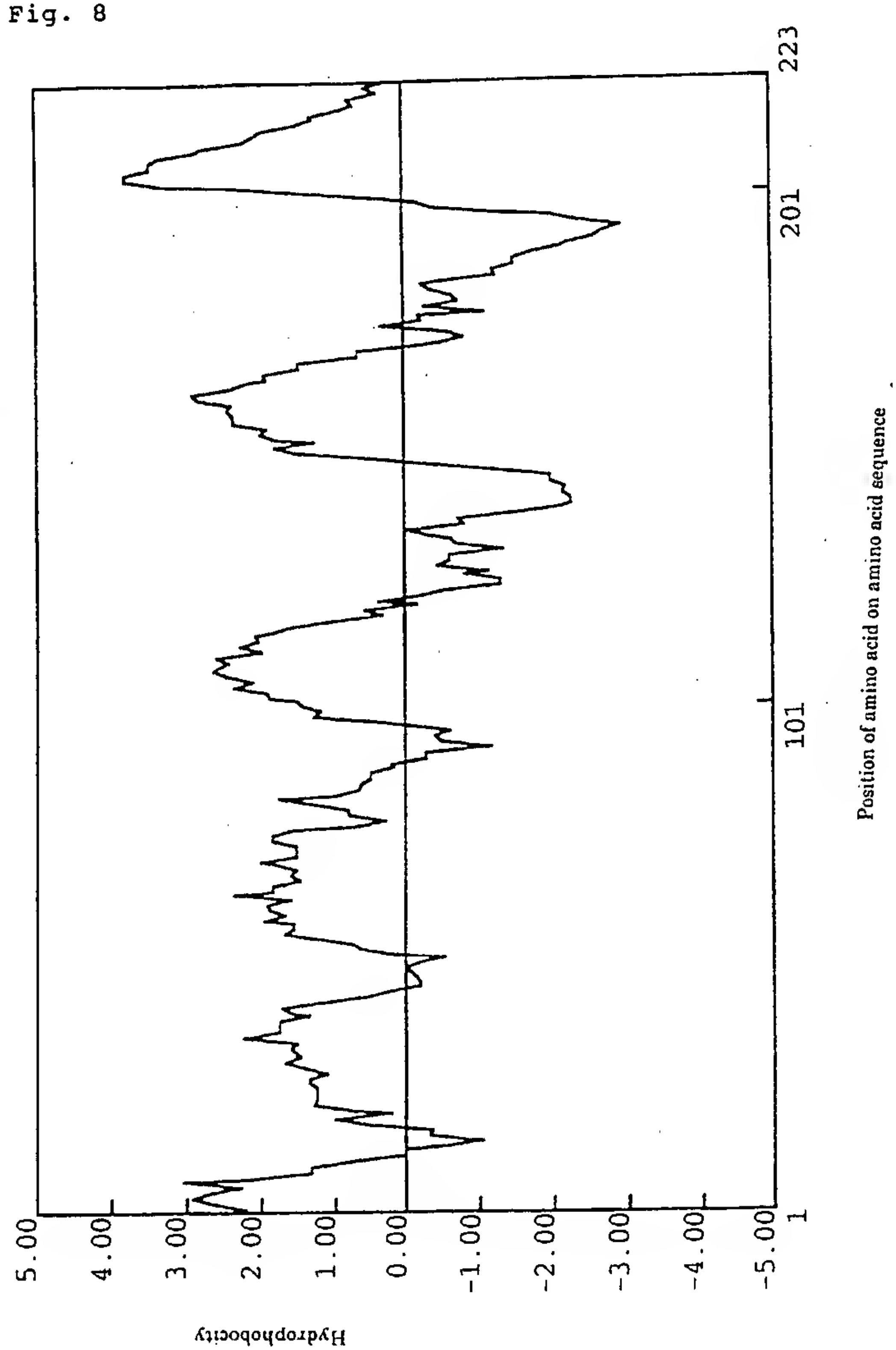
```
                  9                 18                27                36                45                54
5'  GTG GGC ATG GTG GGC AAC ATC CTG CTG CTG CTG GTG ATC GCG CGG GTG CGC CGG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Val Gly Met Val Gly Asn Ile Leu Leu Val Leu Val Ile Ala Arg Val Arg Arg

                 63                72                81                90                99               108
    CTG TAC AAC GTG ACG AAT TTC CTC ATC GGC AAC CTG GCC TTG TCC GAC GTG CTC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Leu Tyr Asn Val Thr Asn Phe Leu Ile Gly Asn Leu Ala Leu Ser Asp Val Leu

                117               126               135               144               153               162
    ATG TGC ACC GCC TGC GTG CCG CTC ACG CTG GCC TAT GCC TTC GAG CCA CGC GGC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Met Cys Thr Ala Cys Val Pro Leu Thr Leu Ala Tyr Ala Phe Glu Pro Arg Gly

                171               180               189               198               207               216
    TGG GTG TTC GGC GGC GGC CTG TGC CAC CTG GTC TTC TTC CTG CAG GCG GTG ACC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Trp Val Phe Gly Gly Gly Leu Cys His Leu Val Phe Phe Leu Gln Ala Val Thr

                225               234               243               252               261               270
    GTG TAT GTG TCG GTG TTC ACG CTC ACC ACC ATC GCA GTG GAC CGC TAC GTG GTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Val Tyr Val Ser Val Phe Thr Leu Thr Thr Ile Ala Val Asp Arg Tyr Val Val

                279               288               297               306               315               324
    CTG CTG CAC CCG CTG AGG CGG CGC ATC TCG CTG CGC CTC AGC GCC TAC GCT GTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Leu Val His Pro Leu Arg Arg Arg Ile Ser Leu Arg Leu Ser Ala Tyr Ala Val

                333               342               351               360               369               378
    CTG GCC ATC TGG GTG CTG TCC GCG GTG CTG GCG CTG CCC GCC GCC GTG CAC ACC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Leu Ala Ile Trp Val Leu Ser Ala Val Leu Ala Leu Pro Ala Ala Val His Thr

                387               396               405               414               423               432
    TAT CAC GTG GAG CTC AAG CCG CAC GAC GTG CGC CTC TGC GAG GAG TTC TGG GGC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Tyr His Val Glu Leu Lys Pro His Asp Val Arg Leu Cys Glu Glu Phe Trp Gly

                441               450               459               468               477               486
    TCC CAG GAG CGC CAG CGC CAG CTC TAC GCC TGG GGG CTG CTG CTG GTG ACC TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Ser Gln Glu Arg Gln Arg Gln Leu Tyr Ala Trp Gly Leu Leu Leu Val Thr Tyr

                495               504               513               522               531               540
    CTG CTC CCT CTG CTG GTG ATC CTC CTG TCT TAC GCC CGG GTG TCA GTG AAG CTC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Leu Leu Pro Leu Leu Val Ile Leu Leu Ser Tyr Ala Arg Val Ser Val Lys Leu

                549               558               567               576               585               594
    CGC AAC CGC CTG GTG CCG GGC CGC GTG ACC CAG AGC CAG GCC GAC TGG GAC CGC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Arg Asn Arg Val Val Pro Gly Arg Val Thr Gln Ser Gln Ala Asp Trp Asp Arg

                603               612               621               630               639               648
    GCT CGG CGC CGG CGC ACC TTC TGC TTG CTG CTG GTG GTG CTG GTG GTG TTC ACC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Ala Arg Arg Arg Arg Thr Phe Cys Leu Leu Val Val Val Val Val Val Phe Thr

                657               666
    CTC TGC TGG CTG CCC TTC TTC 3'
    --- --- --- --- --- --- ---
    Leu Cys Trp Leu Pro Phe Phe
```

Fig. 7

```
                          10         20         30         40         50
p19P2             1 VGMVGNVLLV LVIARVRRLH NVTNFLIGNL ALSDVLMCTA CVPLTLAYAF   50
pG3-2/pG1-10      1 VGMVGNILLV LVIARVRRLY NVTNFLIGNL ALSDVLMCTA CVPLTLAYAF   50

                          60         70         80         90        100
p19P2            51 EPRGWVFGGG LCHLVFFLQP VTVYVSVFTL TTIAVDRYVV LVHPLRRRI-  100
pG3-2/pG1-10     51 EPRGWVFGGG LCHLVFFLQA VTVYVSVFTL TTIAVDRYVV LVHPLRRRIS  100

                         110        120        130        140        150
p19P2           101 ---------- ---------- ---------- ---------- ----------  150
pG3-2/pG1-10    101 LRLSAYAVLA IWVLSAVLAL PAAVHTYHVE LKPHDVRLCE EFWGSQERQR  150

                         160        170        180        190        200
p19P2           151 -----GLLLV TYLLPLLVIL LSYVRVSVKL RNRVVFGCVT QSQADWDRAR  200
pG3-2/pG1-10    151 QLYAWGLLLV TYLLPLLVIL LSYARVSVKL RNRVVFGRVT QSQADWDRAR  200

                         210        220        230        240        250
p19P2           201 RRRTFCLLVV VVVVFAICWL PYY....... .......... ..........  250
pG3-2/pG1-10    201 RRRTFCLLVV VVVVFTLCWL PFF....... .......... ..........  250
```

09/446543

Fig. 8



09/446543

Fig. 9

```
1    CATCGTCAAGCAGATGAAGATCATCCACGAGGATGGCTACTCCGAGGGCCAGCAGAAATT    60
1                                                                    1

61   CTGCCCCTTCTTCCCGCGAGTGCTTTCCCGCTCTCCAAACCCCACTCCCAGGTGGCCATG    120
1                                                             Met    1

121  GCCTCATCGACCACTCGGGGCCCCAGGGTTTCTGACTTATTTTCTGGGCTGCCGCCGGCG    180
2    AlaSerSerThrThrArgGlyProArgValSerAspLeuPheSerGlyLeuProProAla    21

181  GTCACAACTCCCGCCAACCAGAGCGCAGAGGCCTCGGCGGGCAACGGGTCGGTGGCTGGC    240
22   ValThrThrProAlaAsnGlnSerAlaGluAlaSerAlaGlyAsnGlySerValAlaGly    41

241  GCGGACGCTCCAGCCGTCACGCCCTTCCAGAGCCTGCAGCTGGTGCATCAGCTGAAGGGG    300
42   AlaAspAlaProAlaValThrProPheGlnSerLeuGlnLeuValHisGlnLeuLysGly    61

301  CTGATCGTGCTGCTCTACAGCGTCGTGGTGGTCGTGGGGCTGGTGGGCAACTGCCTGCTG    360
62   LeuIleValLeuLeuTyrSerValValValValValGlyLeuValGlyAsnCysLeuLeu    81

361  GTGCTGGTGATCGCGCGGGTGCGCCGGCTGCACAACGTGACGAACTTCCTCATCGGCAAC    420
82   ValLeuValIleAlaArgValArgArgLeuHisAsnValThrAsnPheLeuIleGlyAsn    101

421  CTGGCCTTGTCCGACGTGCTCATGTGCACCGCCTGCGTGCCGCTCACGCTGGCCTATGCC    480
102  LeuAlaLeuSerAspValLeuMetCysThrAlaCysValProLeuThrLeuAlaTyrAla    121

481  TTCGAGCCACGCGGCTGGGTGTTCGGCGGCGGCCTGTGCCACCTGGTCTTCTTCCTGCAG    540
122  PheGluProArgGlyTrpValPheGlyGlyGlyLeuCysHisLeuValPhePheLeuGln    141

541  CCGGTCACCGTCTATGTGTCGGTGTTCACGCTCACCACCATCGCAGTGGACCGCTACGTC    600
142  ProValThrValTyrValSerValPheThrLeuThrThrIleAlaValAspArgTyrVal    161

601  GTGCTGGTGCACCCGCTGAGGCGGCGCATCTCGCTGCGCCTCAGCGCCTACGCTGTGCTG    660
162  ValLeuValHisProLeuArgArgArgIleSerLeuArgLeuSerAlaTyrAlaValLeu    181

661  GCCATCTGGGCGCTGTCCGCGGTGCTGGCGCTGCCCGCCGCCGTGCACACCTATCACGTG    720
182  AlaIleTrpAlaLeuSerAlaValLeuAlaLeuProAlaAlaValHisThrTyrHisVal    201

721  GAGCTCAAGCCGCACGACGTGCGCCTCTGCGAGGAGTTCTGGGGCTCCCAGGAGCGCCAG    780
202  GluLeuLysProHisAspValArgLeuCysGluGluPheTrpGlySerGlnGluArgGln    221

781  CGCCAGCTCTACGCCTGGGGGCTGCTGCTGGTCACCTACCTGCTCCCTCTGCTGGTCATC    840
222  ArgGlnLeuTyrAlaTrpGlyLeuLeuLeuValThrTyrLeuLeuProLeuLeuValIle    241

841  CTCCTGTCTTACGTCCGGGTGTCAGTGAAGCTCCGCAACCGCGTGGTGCCGGGCTGCGTG    900
242  LeuLeuSerTyrValArgValSerValLysLeuArgAsnArgValValProGlyCysVal    261

901  ACCCAGAGCCAGGCCGACTGGGACCGCGCTCGGCGCCGGCGCACCTTCTGCTTGCTGGTG    960
262  ThrGlnSerGlnAlaAspTrpAspArgAlaArgArgArgArgThrPheCysLeuLeuVal    281

961  GTGGTCGTGGTGGTGTTCGCCGTCTGCTGGCTGCCGCTGCACGTCTTCAACCTGCTGCGG    1020
282  ValValValValValPheAlaValCysTrpLeuProLeuHisValPheAsnLeuLeuArg    301

1021 GACCTCGACCCCCACGCCATCGACCCTTACGCCTTTGGGCTGGTGCAGCTGCTCTGCCAC    1080
302  AspLeuAspProHisAlaIleAspProTyrAlaPheGlyLeuValGlnLeuLeuCysHis    321

1081 TGGCTCGCCATGAGTTCGGCCTGCTACAACCCCTTCATCTACGCCTGGCTGCACGACAGC    1140
322  TrpLeuAlaMetSerSerAlaCysTyrAsnProPheIleTyrAlaTrpLeuHisAspSer    341

1141 TTCCGCGAGGAGCTGCGCAAACTGTTGGTCGCTTGGCCCCGCAAGATAGCCCCCCATGGC    1200
342  PheArgGluGluLeuArgLysLeuLeuValAlaTrpProArgLysIleAlaProHisGly    361

1201 CAGAATATGACCGTCAGCGTGGTCATCTGATGCCACTTAGCCAGGCCTTGGTCAAGGAGC    1260
362  GlnAsnMetThrValSerValValIle***                                  371

1261 TCCACTTCAACTGGCCTCCTAGGGCACCACTCGAGGTCAATCTGGTGCTTATTCTCAGCA    1320
                                                                     371

1321 CCAGAGCTAGC                                                     1331
                                                                     371
```

Fig. 10

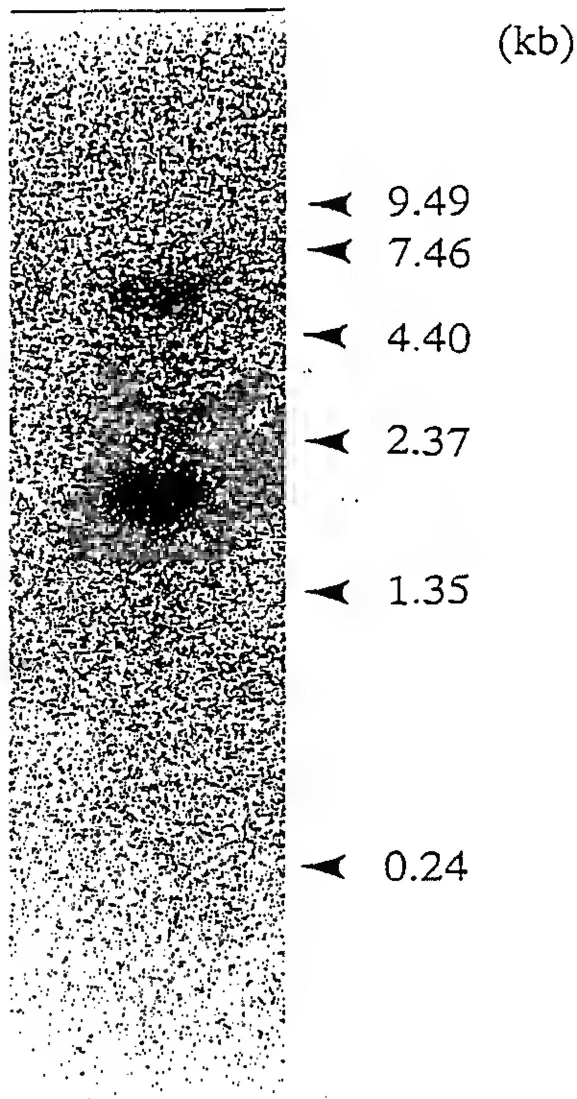
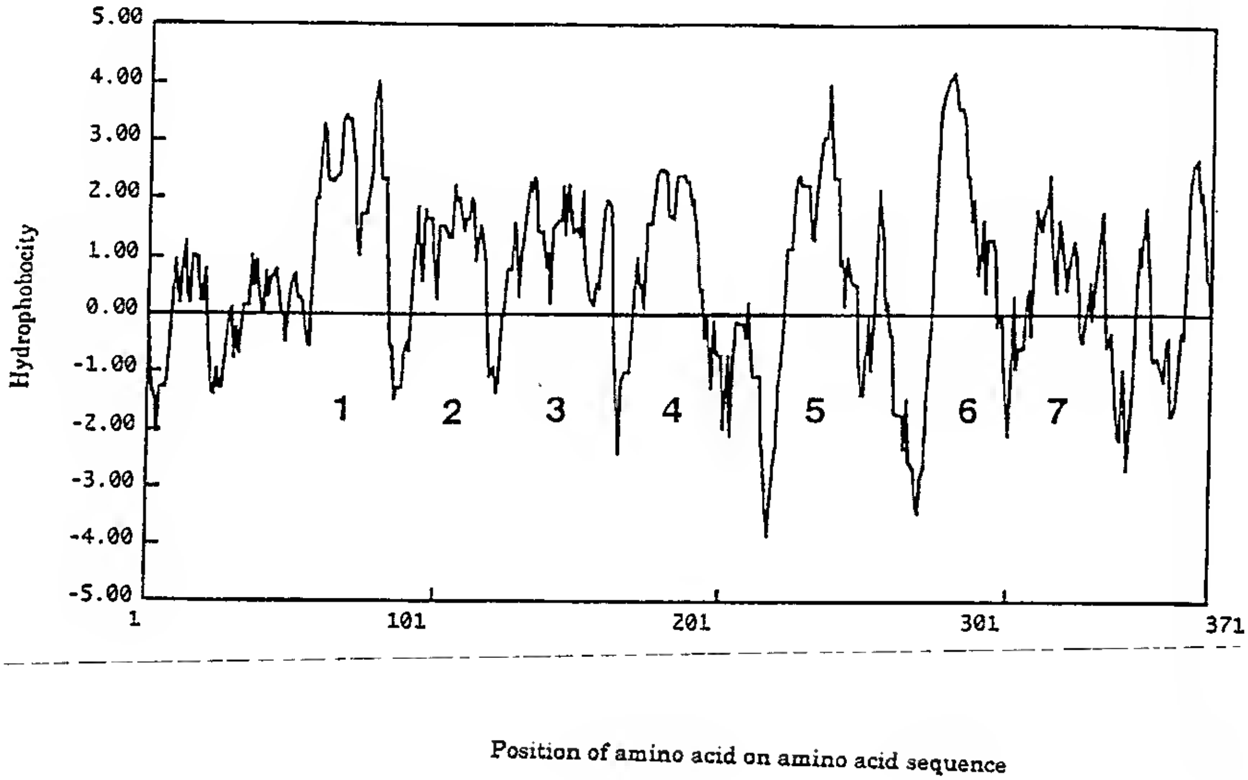


Fig. 11


5.00
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
Hydrophobocity
1
2
3
4
5
6
7
1
101
201
301
371
Position of amino acid on amino acid sequence

09/446543

Fig. 12

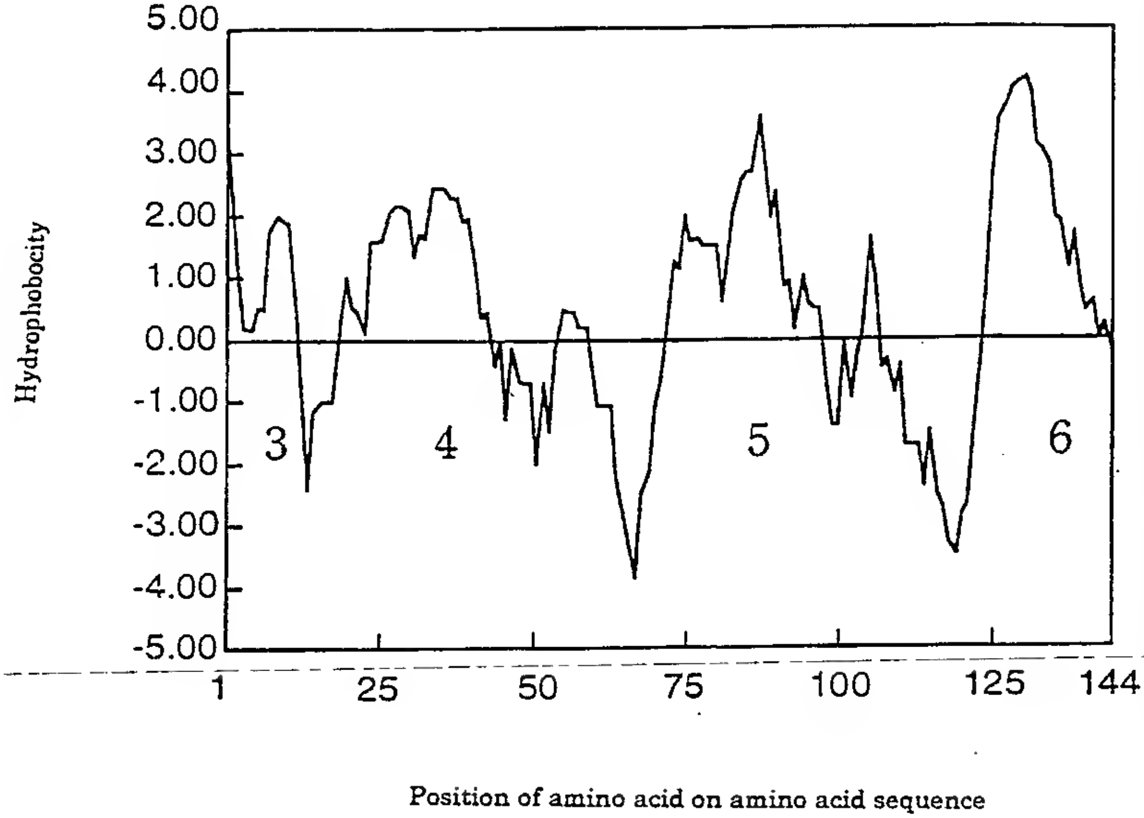
```
                 9              18              27              36              45              54
5' CTG TGT GTC ATC GCG GTG GAT AGG TAC GTG GTT CTG GTG CAC CCG CTA CGT CGG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu Cys Val Ile Ala Val Asp Arg Tyr Val Val Leu Val His Pro Leu Arg Arg

                63              72              81              90              99             108
   CGC ATT TCA CTG AGG CTC AGC GCC TAC GCG GTG CTG GGC ATC TGG GCT CTA TCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Arg Ile Ser Leu Arg Leu Ser Ala Tyr Ala Val Leu Gly Ile Trp Ala Leu Ser

               117             126             135             144             153             162
   GCA GTG CTG GCG CTG CCG GCC GCG GTG CAC ACC TAC CAT GTG GAG CTC AAG CCC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Ala Val Leu Ala Leu Pro Ala Ala Val His Thr Tyr His Val Glu Leu Lys Pro

               171             180             189             198             207             216
   CAC GAC GTG AGC CTC TGC GAG GAG TTC TGG GGC TCG CAG GAG CGC CAA CGC CAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   His Asp Val Ser Leu Cys Glu Glu Phe Trp Gly Ser Gln Glu Arg Gln Arg Gln

               225             234             243             252             261             270
   ATC TAC GCC TGG GGG CTG CTT CTG GGC ACC TAT TTG CTC CCC CTG CTG GCC ATC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Ile Tyr Ala Trp Gly Leu Leu Leu Gly Thr Tyr Leu Leu Pro Leu Leu Ala Ile

               279             288             297             306             315             324
   CTC CTG TCT TAC GTA CGG GTG TCA GTG AAG CTG AGG AAC CGC GTG GTG CCT GGC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu Leu Ser Tyr Val Arg Val Ser Val Lys Leu Arg Asn Arg Val Val Pro Gly

               333             342             351             360             369             378
   AGC GTG ACC CAG AGT CAA GCT GAC TGG GAC CGA GCG CGT CGC CGC CGC ACT TTC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Ser Val Thr Gln Ser Gln Ala Asp Trp Asp Arg Ala Arg Arg Arg Arg Thr Phe

               387             396             405             414             423             432
   TGT CTG CTG GTG GTG GTG GTG GTA GTG TTC ACG CTC TGC TGG CTG CCC TTC TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Cys Leu Leu Val Val Val Val Val Val Phe Thr Leu Cys Trp Leu Pro Phe Tyr

   CT 3'
   --
```

Fig. 13

```
                         10         20         30         40         50
p19P2            1 VGMVGNVLLV LVIARVRRLH NVTNFLIGNL ALSDVLMCTA CVPLTLAYAF   50
pG3-2/pG1-10     1 VGMVGNILLV LVIARVRRLY NVTNFLIGNL ALSDVLMCTA CVPLTLAYAF   50
p5S38          -79 .......... .......... .......... .......... ..........  -30

                         60         70         80         90        100
p19P2           51 EPRGWVFGGG LCHLVFFLQP VTVYVSVFTL TTIAVDRYVV LVHPLRRRI-  100
pG3-2/pG1-10    51 EPRGWVFGGG LCHLVFFLQA VTVYVSVFTL TTIAVDRYVV LVHPLRRRIS  100
p5S38          -29 .......... .......... .........L CVIAVDRYVV LVHPLRRRIS   21

                        110        120        130        140        150
p19P2          101 ---------- ---------- ---------- ---------- ----------  150
pG3-2/pG1-10   101 LRLSAYAVLA IWVLSAVLAL PAAVHTYHVE LKPHDVRLCE EFWGSQERQR  150
p5S38           22 LRLSAYAVLG IWALSAVLAL PAAVHTYHVE LKPHDVSLCE EFWGSQERQR   71

                        160        170        180        190        200
p19P2          151 -----GLLLV TYLLPLLVIL LSYVRVSVKL RNRVVPGEVT QSQADWDRAR  200
pG3-2/pG1-10   151 QLYAWGLLLV TYLLPLLVIL LSYARVSVKL RNRVVPGAVT QSQADWDRAR  200
p5S38           72 QIYAWGLLLG TYLLPLLAIL LSYVRVSVKL RNRVVPGSVT QSQADWDRAR  121

                        210        220        230        240        250
p19P2          201 RRRTFCLLVW VVVVFAICWL PYY....... .......... ..........  250
pG3-2/pG1-10   201 RRRTFCLLVV VVVVFTLCWL PFF....... .......... ..........  250
p5S38          122 RRRTFCLLVV VVVVFTLCWL PFY....... .......... ..........  171
```

09/446543

Fig. 14


5.00
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
Hydrophobocity
3
4
5
6
1
25
50
75
100
125
144
Position of amino acid on amino acid sequence

09/446543

Fig. 15

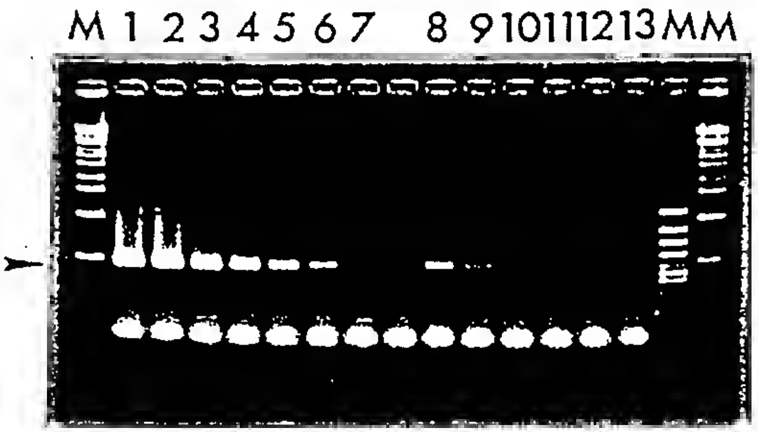


Fig. 16

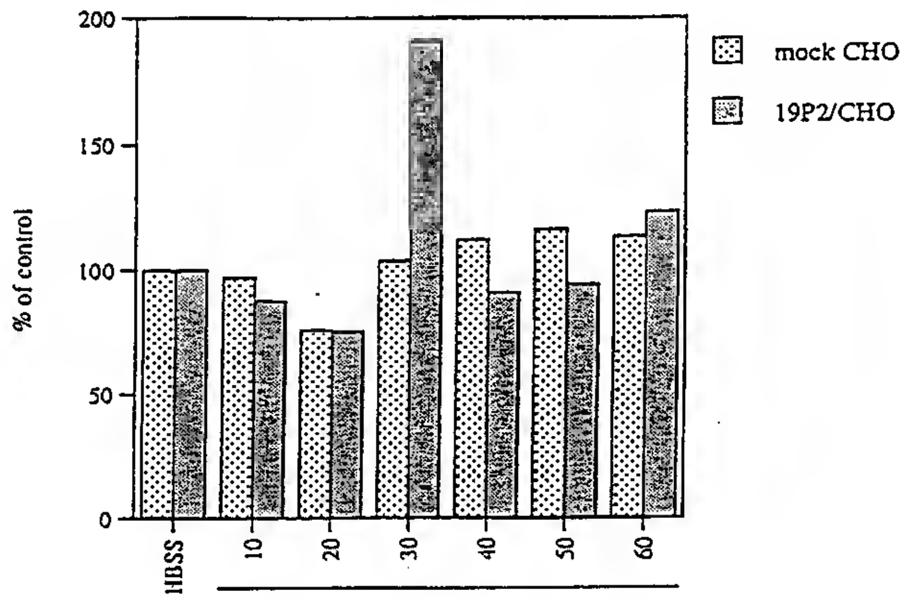
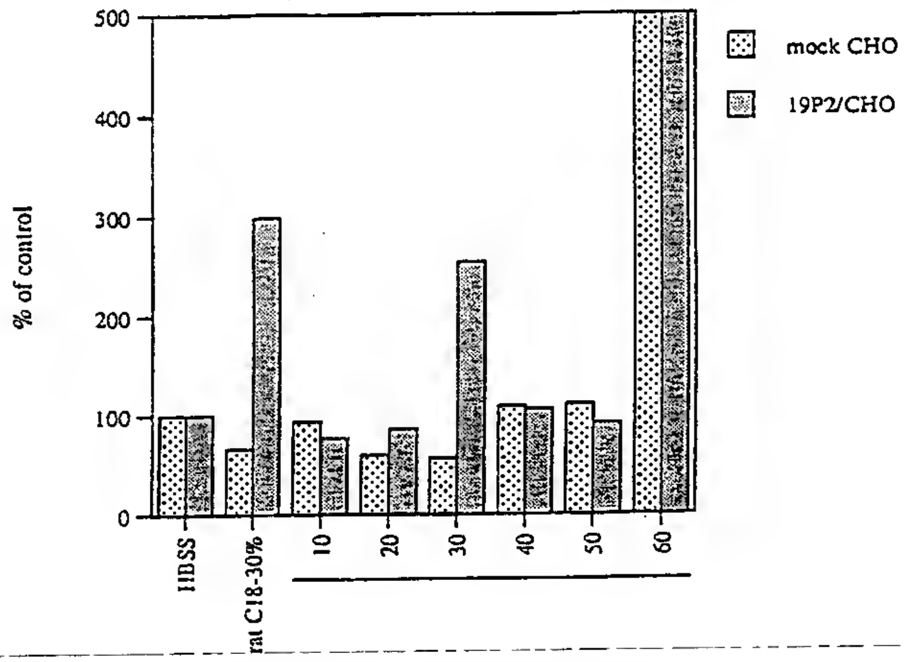

200
150
100
50
0
% of control
mock CHO
19P2/CHO
HBSS
10
20
30
40
50
60

Fig. 17



500
400
300
200
100
0
% of control
mock CHO
19P2/CHO
HBSS
rat C18-30%
10
20
30
40
50
60

Fig. 18

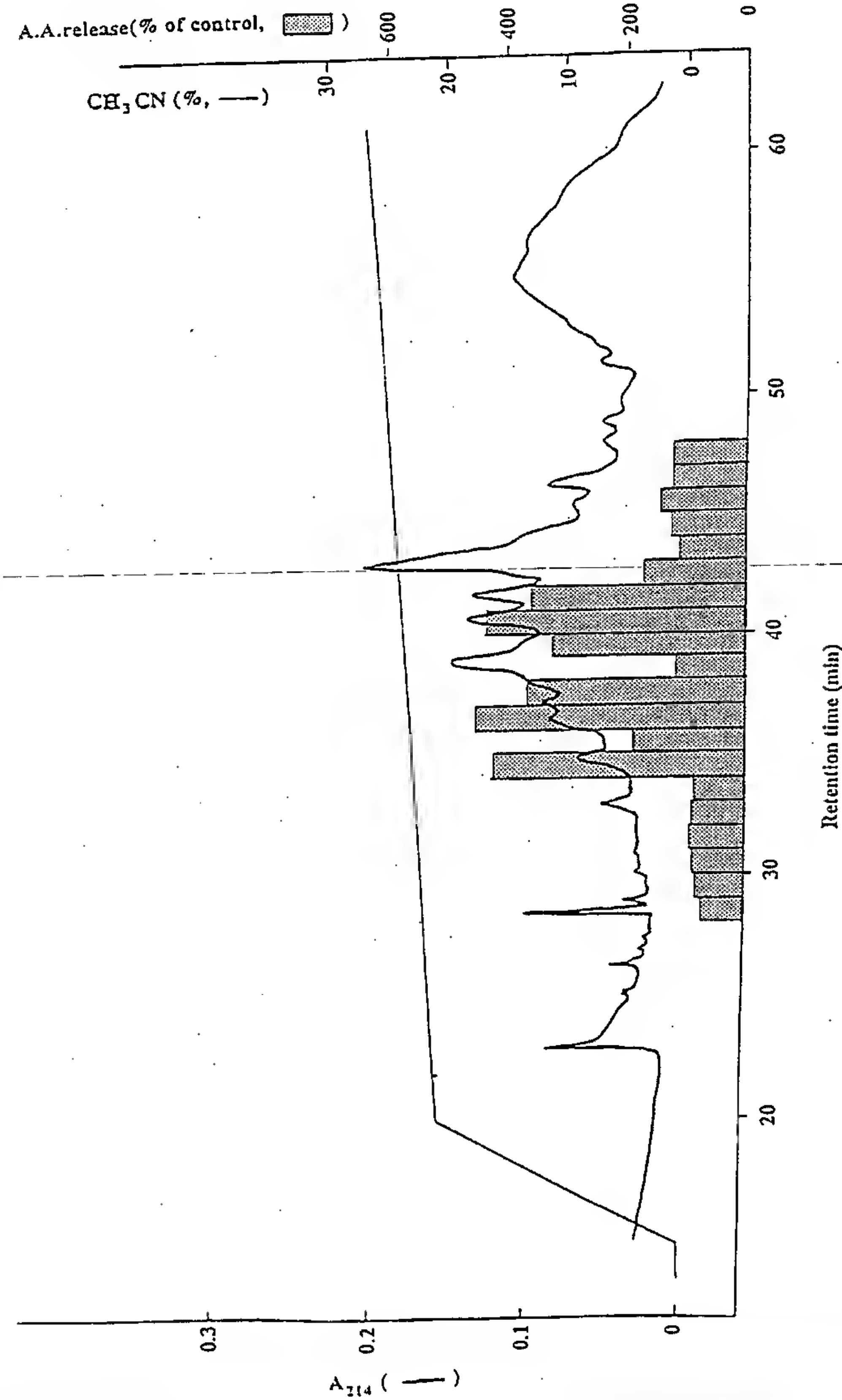
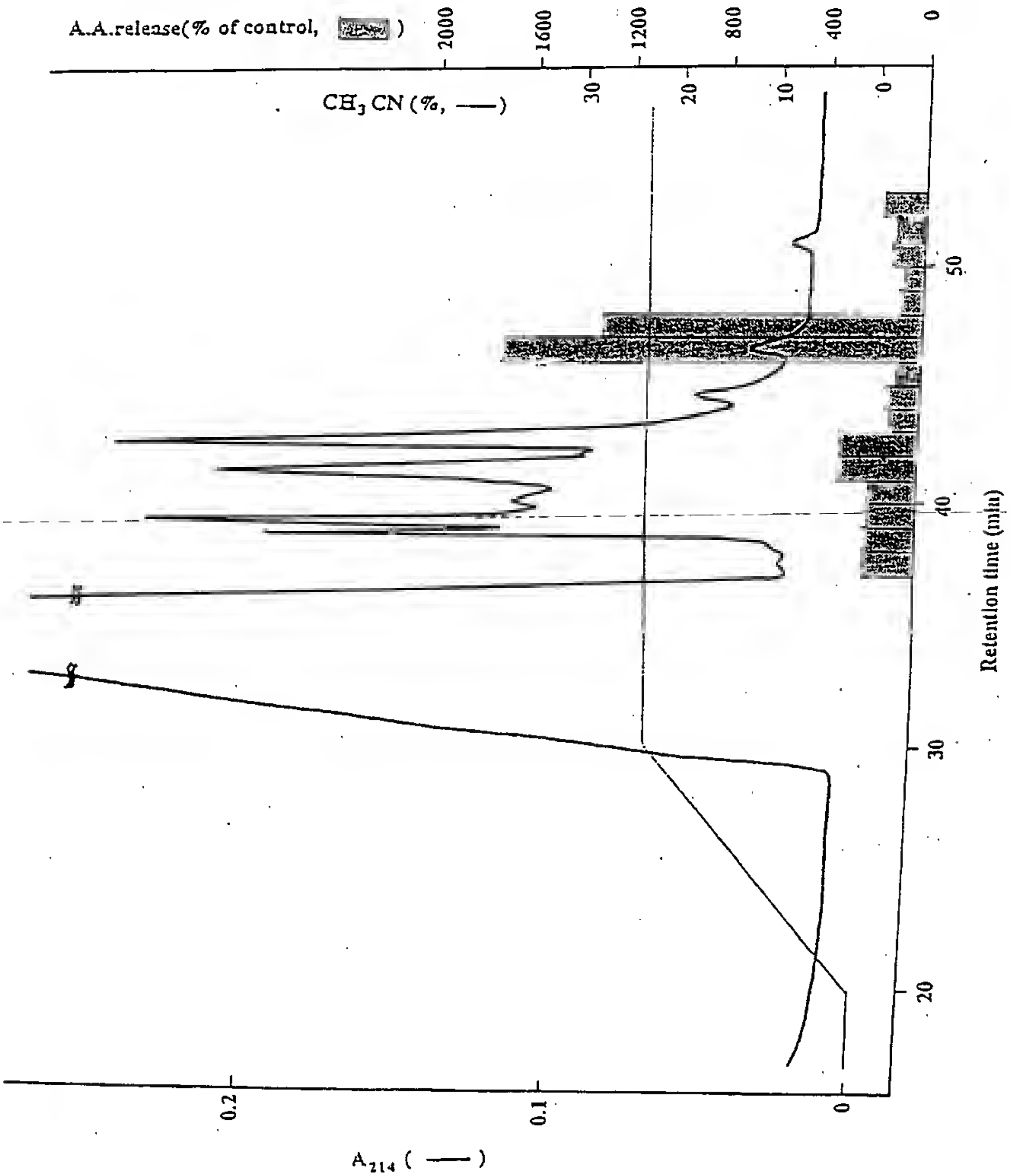
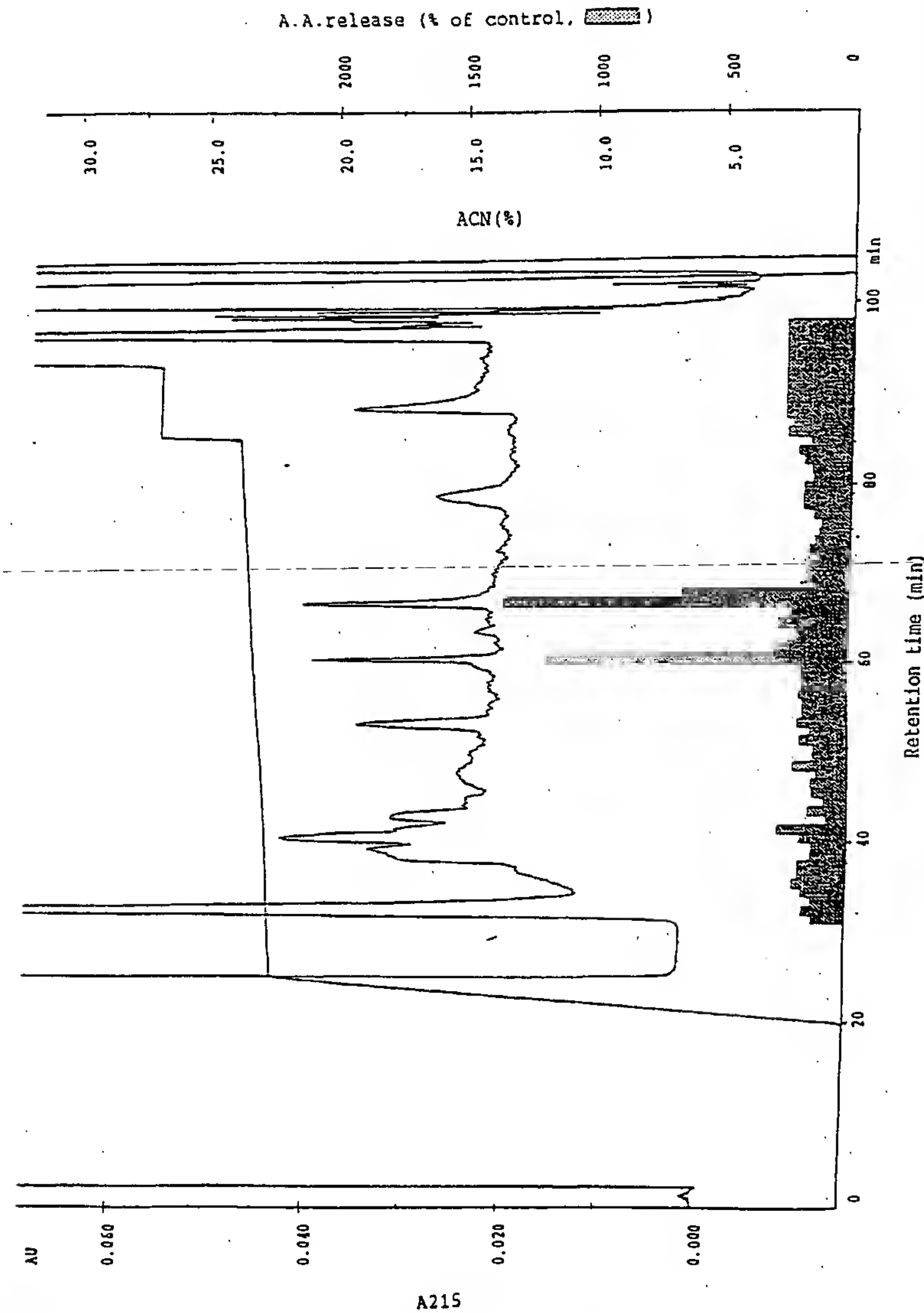

A.A.release(% of control,)
600
400
200
0
CH$_3$CN (%, —)
30
20
10
0
60
50
40
30
20
Retention time (min)
0.3
0.2
0.1
0
A$_{214}$ (—)

Fig. 19


A.A.release(% of control,)
2000
1600
1200
800
400
0
CH_3CN (%, —)
30
20
10
0
Retention time (min)
20
30
40
50
A_{214} (—)
0.2
0.1
0

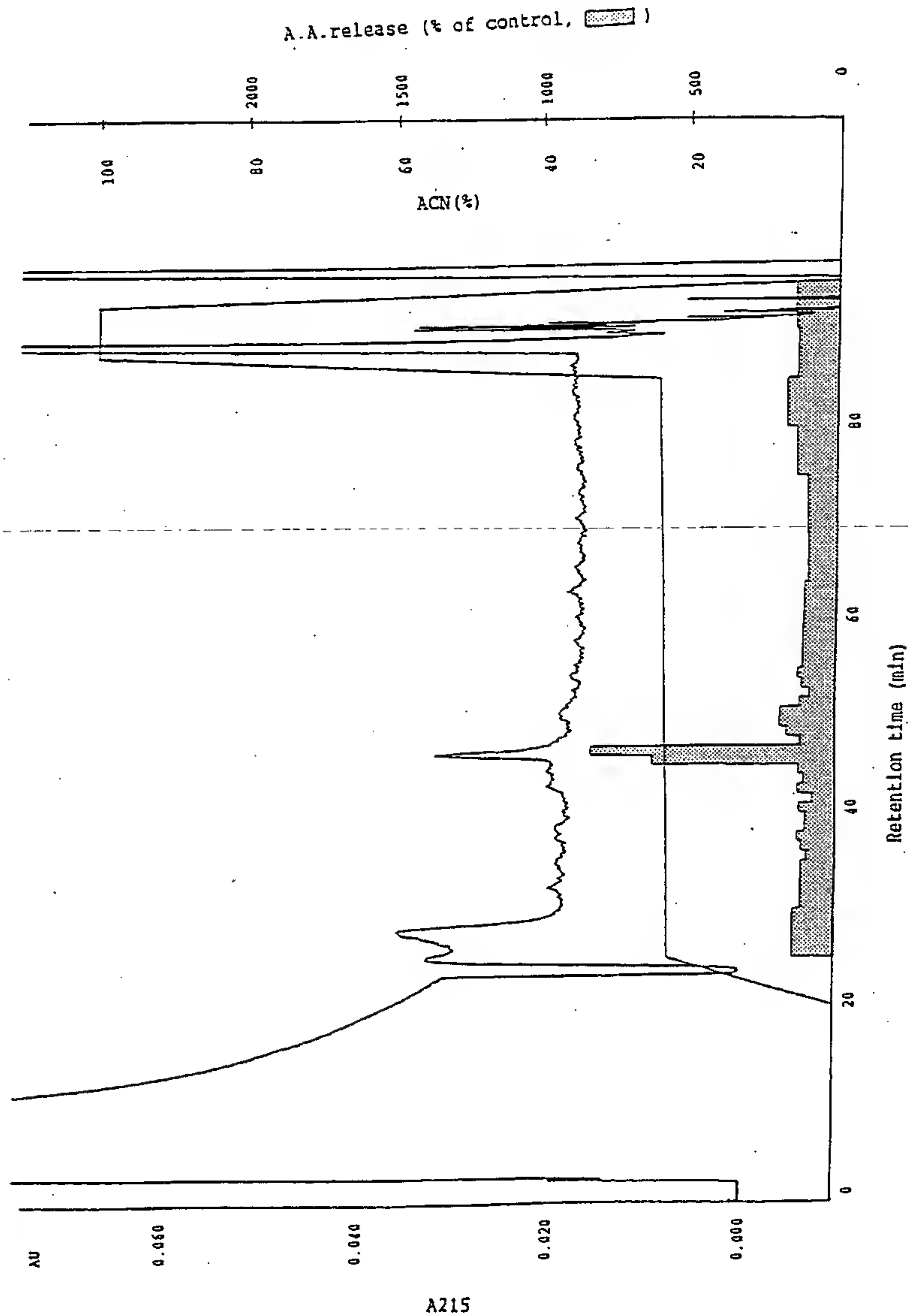
09/446543

Fig. 20



09/446543

Fig. 21



09/446543

Fig. 22

```
    P5-1
    ----------------------------------------->
                  9        18        27        36        45        54
5'  GCC CAC CAG CAC TCC ATG GAG ATC CGC ACC CCC GAC ATC AAC CCT GCC TGG TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Ala His Gln His Ser Met Glu Ile Arg Thr Pro Asp Ile Asn Pro Ala Trp Tyr
                                                                        <--

                 63        72
    GCG GGC CGT GGG ATC CGG CCC G 3'
    --- --- --- --- --- --- --- -
    Ala Gly Arg Gly Ile Arg Pro
    ---------------------------
          P3-2
```

Fig. 23

```
  1  GTGGAATGAAGGCGGTGGGGGCCTGGCTCCTCTGCCTGCTGCTGCTGGGCCTGGCCCTG    59
  1       MetLysAlaValGlyAlaTrpLeuLeuCysLeuLeuLeuLeuGlyLeuAlaLeu     18

 60  CAGGGGGCTGCCAGCAGAGCCCACCAGCACTCCATGGAGATCCGCACCCCCGACATCAAC  119
 19  GlnGlyAlaAlaSerArgAlaHisGlnHisSerMetGluIleArgThrProAspIleAsn   38
                                            <----------------------
                                                     PDN

120  CCTGCCT                                                        126
 39  ProAla                                                          40
     ------
```

Fig. 24(a)

```
  1 GTGGAATGAAGGCGGTGGGGGCCTGGCTCCTCTGCCTGCTGCTGCTGGGCCTGGCCCTG   59
  1      MetLysAlaValGlyAlaTrpLeuLeuCysLeuLeuLeuLeuGlyLeuAlaLeu    18

 60 CAGGGGGCTGCCAGCAGAGCCCACCAGCACTCCATGGAGATCCGCACCCCCGACATCAAC 119
 19 GlnGlyAlaAlaSerArgAlaHisGlnHisSerMetGluIleArgThrProAspIleAsn  38

120 CCTGCCTGGTACGCRGGCCGTGGGATCCGGCCCGTGGGCCGCTTCGGCCGGCGAAGAGCT 179
 39 ProAlaTrpTyrAlaGlyArgGlyIleArgProValGlyArgPheGlyArgArgArgAla  58

180 GCCCCGGGGGACGGACCCAGGCCTGGCCCCCGGCGTGTGCCGGCCTGCTTCCGCCTGGAA 239
 59 AlaProGlyAspGlyProArgProGlyProArgArgValProAlaCysPheArgLeuGlu  78

240 GGCGGYGCTGAGCCCTCCCGAGCCCTCCCGGGGCGGCTGACGGCCCAGCTGGTCCAGGAA 299
 79 GlyGlyAlaGluProSerArgAlaLeuProGlyArgLeuThrAlaGlnLeuValGlnGlu  98

300 TAACAGCGGGAGCCTGCCCCCCACCCCTCCTCCTCCACCAGCCACCTTCCCTCCAGTCCT 359
 98                                                               98

360 AATAAAAGCAGCTGGCTTGTT                                        380
 98                                                               98
```

Fig. 24(b)

```
  1  GTGGAATGAAGGCGGTGGGGGCCTGGCTCCTCTGCCTGCTGCTGCTGGGCCTGGCCCTG     59
  1        MetLysAlaValGlyAlaTrpLeuLeuCysLeuLeuLeuLeuGlyLeuAlaLeu     18

 60  CAGGGGGCTGCCAGCAGAGCCCACCAGCACTCCATGGAGATCCGCACCCCCGACATCAAC    119
 19  GlnGlyAlaAlaSerArgAlaHisGlnHisSerMetGluIleArgThrProAspIleAsn     38

120  CCTGCCTGGTACGCRGGCCGTGGGATCCGGCCCGTGGGCCGCTTCGGCCGGCGAAGAGCT    179
 39  ProAlaTrpTyrAlaGlyArgGlyIleArgProValGlyArgPheGlyArgArgArgAla     58

180  GCCCTGGGGGACGGACCCAGGCCTGGCCCCCGGCGTGTGCCGGCCTGCTTCCGCCTGGAA    239
 59  AlaLeuGlyAspGlyProArgProGlyProArgArgValProAlaCysPheArgLeuGlu     78

240  GGCGGYGCTGAGCCCTCCCGAGCCCTCCCGGGGCGGCTGACGGCCCAGCTGGTCCAGGAA    299
 79  GlyGlyAlaGluProSerArgAlaLeuProGlyArgLeuThrAlaGlnLeuValGlnGlu     98

300  TAACAGCGGGAGCCTGCCCCCCACCCCTCCTCCTCCACCAGCCACCTTCCCTCCAGTCCT    359
 98                                                                   98

360  AATAAAAGCAGCTGGCTTGTT                                           380
 98                                                                   98
```

Fig. 25

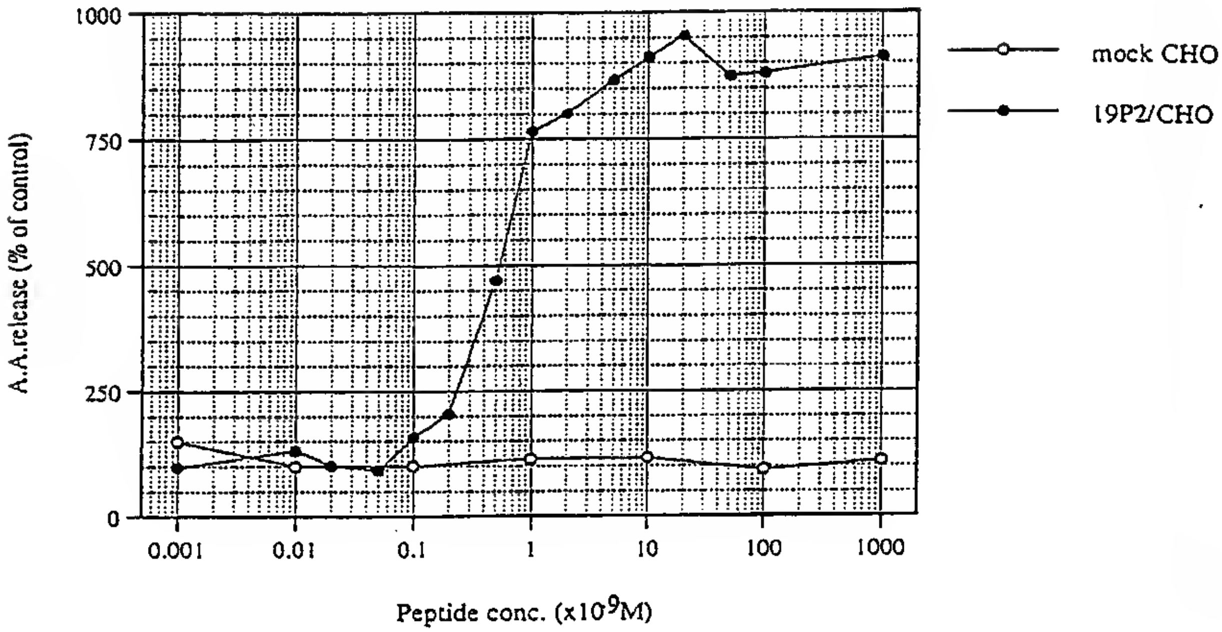
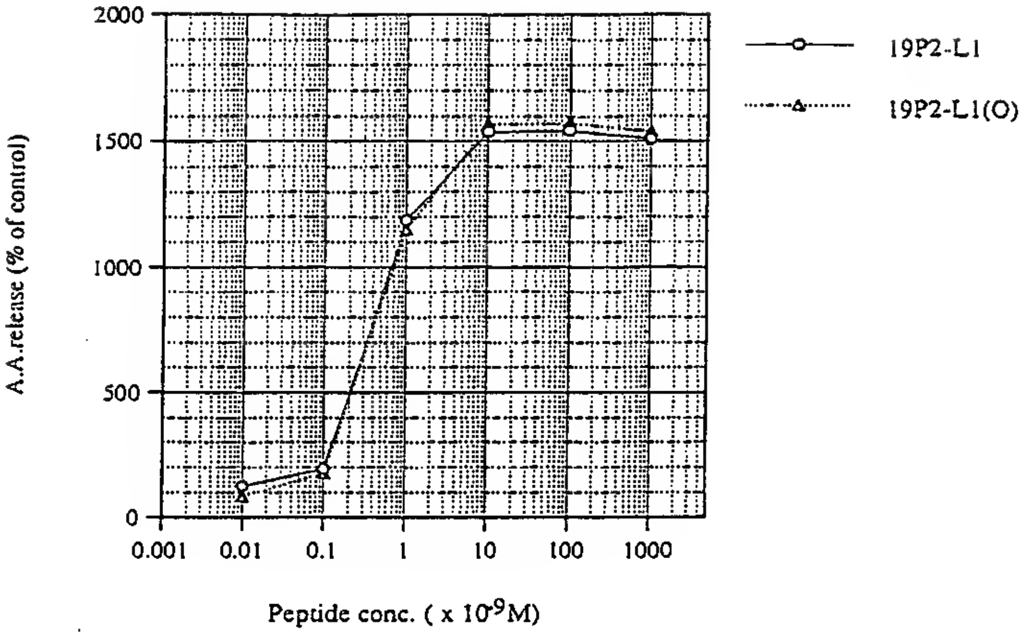
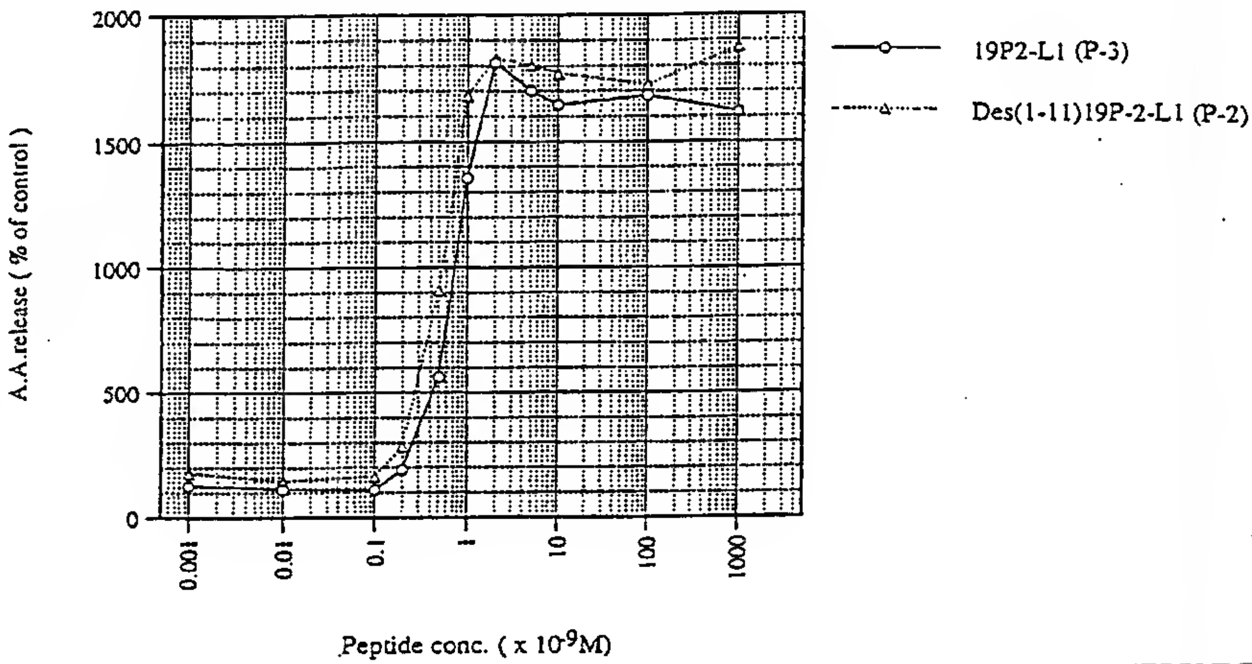

1000
750
500
250
0
A.A.release (% of control)
0.001
0.01
0.1
1
10
100
1000
Peptide conc. (x10⁹M)
mock CHO
19P2/CHO

Fig. 26



2000
1500
1000
500
0
A.A.release (% of control)
0.001
0.01
0.1
1
10
100
1000
Peptide conc. (x 10-9M)
19P2-L1
19P2-L1(O)

Fig. 27



2000
1500
1000
500
0
A.A.release (% of control)
0.001
0.01
0.1
1
10
100
1000
Peptide conc. (x 10^{-9}M)
19P2-L1 (P-3)
Des(1-11)19P-2-L1 (P-2)

Fig. 28

Fig. 29

```
        10         20         30         40         50         60
ATGAAGGCGG TGGGGGCCTG GCTCCTCTGC CTGCTGCTGC TGGGCCTGGC CCTGCAGGGG

        70         80         90        100        110        120
GCTGCCAGCA GAGCCCACCA GCACTCCATG GAGATCCGCA GTGAGTGTCT AGCCCCGCCC

       130        140        150        160        170        180
CTGCCCCCAG GGGTCACAGG GGGGGCCTGG CCACTTCCTG GGCTGGGACA TCCTTGCTAA

       190        200        210        220        230        240
GCATCCTGGG GTTGGGGTTT GGCCTCCTGT TCCCCAGACC CTTCCCCCAG GTGGCCCGGA

       250        260        270        280        290        300
CAGGTGCTCC CAAGGGTCCC GGCCCAGCAC ACGGGGGAGG GTCACTCCTC ACCACACGGG

       310        320        330        340        350        360
TGGCCTGGGG CTGAGTGCAC GTCACCCATG AGAACGGGGC TGTGAGGACA GGAAAGGAAG

       370        380        390        400        410        420
GGGAGTGTGT CCTGGTGTGA GTCTGAAATC CTACTTCCCA AAGCCACCCC AGCACCAGAA

       430        440        450        460        470        480
ATGGGCGCTC CGGGTGAACC TCCTGTGCGG GTGGGTGGTC CTGGCATGGC CTGGGCGACA

       490        500        510        520        530        540
GGCAGCCATG AGCTGAGCAC ACACCCGGCC CGGCCACCAG GGCTGTATGC TCCAGGGCAC

       550        560        570        580        590        600
AGGCCTCCAT GCGCTCTTCT CTCTCTTTCC AGCCCCCGAC ATCAACCCTG CCTGGTACGC

       610        620        630        640        650        660
AGGCCGTGGG ATCCGGCCCG TGGGCCGCTT CGGCCGGCGA AGAGCTGCCC TGGGGGACGG

       670        680        690        700        710        720
ACCCAGGCCT GGCCCCCGGC GTGTGCCGGC CTGCTTCCGC CTGGAAGGCG GTGCTGAGCC

       730        740        750        760        770        780
CTCCCGAGCC CTCCCGGGGC GGCTGACGGC CCAGCTGGTC CAGGAATAA. ..........
```

09/446543

Fig. 30

```
                     10         20         30         40         50
genome    1 ATGAAGGCGG TGGGGGCCTG GCTGCTCTGC CTGCTGCTGC TGGGCCTGGC   50
cDNA      1 ATGAAGGCGG TGGGGGCCTG GCTGCTCTGC CTGCTGCTGC TGGGCCTGGC   50

                     60         70         80         90        100
genome   51 CCTGCAGGGG GCTGCCAGCA GAGCCCACCA GCACTGCATG GAGATCCGCA  100
cDNA     51 CCTGCAGGGG GCTGCCAGCA GAGCCCACCA GCACTGCATG GAGATCCGCA  100

                    110        120        130        140        150
genome  101 GTGAGTGTCT AGCCCCGCCC CTGCCCCCAG GGGTCACAGG GGGGGCCTGG  150
cDNA    101 ---------- ---------- ---------- ---------- ----------  150

                    160        170        180        190        200
genome  151 CCACTTCCTG GGCTGGGACA TCCTTGCTAA GCATCCTGGG GTTGGGGTTT  200
cDNA    151 ---------- ---------- ---------- ---------- ----------  200

                    210        220        230        240        250
genome  201 GGCCTGCTGT TCCCCAGACC CTTCCCCCAG GTGGCCCGGA CAGGTGCTCC  250
cDNA    201 ---------- ---------- ---------- ---------- ----------  250

                    260        270        280        290        300
genome  251 CAAGGGTCCC GGGCCAGCAC ACGGGGGAGG GTCACTGCTG ACCACACGGG  300
cDNA    251 ---------- ---------- ---------- ---------- ----------  300

                    310        320        330        340        350
genome  301 TGGCCTGGGG CTGAGTGCAC GTCACCCATG AGAACGGGGC TGTGAGGACA  350
cDNA    301 ---------- ---------- ---------- ---------- ----------  350

                    360        370        380        390        400
genome  351 GGAAAGGAAG GGGAGTGTGT CCTGGTGTGA GTCTGAAATC CTACTTCCCA  400
cDNA    351 ---------- ---------- ---------- ---------- ----------  400

                    410        420        430        440        450
genome  401 AAGCCACCCC AGCACCAGAA ATGGGCGCTC CGGGTGAACC TCCTGTGCGG  450
cDNA    401 ---------- ---------- ---------- ---------- ----------  450

                    460        470        480        490        500
genome  451 GTGGGTGGTC CTGGCATGGC CTGGGCGACA GGCAGCCATG AGCTGAGCAC  500
cDNA    451 ---------- ---------- ---------- ---------- ----------  500

                    510        520        530        540        550
genome  501 ACACCCGGCC CGGCCACCAG GGCTGTATGC TCCAGGGCAC AGGCCTCCAT  550
cDNA    501 ---------- ---------- ---------- ---------- ----------  550

                    560        570        580        590        600
genome  551 GCGCTCTTCT CTCTCTTTCC AGCCCCCGAC ATCAACCCTG CCTGGTACGC  600
cDNA    551 ---------- ---------- --CCCCCGAC ATCAACCCTG CCTGGTACGC  600

                    610        620        630        640        650
genome  601 AGGCCGTGGG ATCCGGCCCG TGGGCCGCTT CGGCCGGCGA AGAGCTGCCC  650
cDNA    601 GGGCCGTGGG ATCCGGCCCG TGGGCCGCTT CGGCCGGCGA AGAGCTGCCC  650

                    660        670        680        690        700
genome  651 TGGGGGACGG ACCCAGGCCT GGCCCCCGGC GTGTGCCGGC CTGCTTCCGC  700
cDNA    651 CGGGGGACGG ACCCAGGCCT GGCCCCCGGC GTGTGCCGGC CTGCTTCCGC  700

                    710        720        730        740        750
genome  701 CTGGAAGGCG GTGCTGAGCC CTCCCGAGCC CTGCCGGGGC GGCTGACGGC  750
cDNA    701 CTGGAAGGCG GCGCTGAGCC CTCCCGAGCC CTCCCGGGGC GGCTGACGGC  750

                    760        770        780        790        800
genome  751 CCAGCTGGTC CAGGAATAA. .......... .......... ..........  800
cDNA    751 CCAGCTGGTC CAGGAATAA. .......... .......... ..........  800
```

09/446543

Fig. 31

```
                9           18          27          36          45          54
5'  ATG AAG GCG GTG GGG GCC TGG CTC CTC TGC CTG CTG CTG CTG GGC CTG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   K   A   V   G   A   W   L   L   C   L   L   L   L   G   L   A   L

                63          72          81          90          99         108
    CAG GGG GCT GCC AGC AGA GCC CAC CAG CAC TCC ATG GAG ATC CGC ACC CCC GAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     Q   G   A   A   S   R   A   H   Q   H   S   M   E   I   R   T   P   D

               117         126         135         144         153         162
    ATC AAC CCT GCC TGG TAC GCA GGC CGT GGG ATC CGG CCC GTG GGC CGC TTC GGC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     I   N   P   A   W   Y   A   G   R   G   I   R   P   V   G   R   F   G

               171         180         189         198         207         216
    CGG CGA AGA GCT GCC CTG GGG GAC GGA CCC AGG CCT GGC CCC CGG CGT GTG CCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   R   R   A   A   L   G   D   G   P   R   P   G   P   R   R   V   P

               225         234         243         252         261         270
    GCC TGC TTC CGC CTG GAA GGC GGT GCT GAG CCC TCC CGA GCC CTC CCG GGG CGG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     A   C   F   R   L   E   G   G   A   E   P   S   R   A   L   P   G   R

               279         288         297
    CTG ACG GCC CAG CTG GTC CAG GAA TAA 3'
    --- --- --- --- --- --- --- --- ---
     L   T   A   Q   L   V   Q   E   *
```

Fig. 32

```
  1 GGCATCATCCAGGAAGACGGAGCATGGCCCTGAAGACGTGGCTTCTGTGCTTGCTGCTG    59
  1                                MetAlaLeuLysThrTrpLeuLeuCysLeuLeuLeu    12

 60 CTAAGCTTGGTCCTCCCAGGGGCTTCCAGCCGAGCCCACCAGCACTCCATGGAGACAAGA   119
 13 LeuSerLeuValLeuProGlyAlaSerSerArgAlaHisGlnHisSerMetGluThrArg    32

120 ACCCCTGATATCAATCCTGCCTGGTACACGGGCCGCGGATCAGGCCTGTGGGCCGCTTC   179
 33 ThrProAspIleAsnProAlaTrpTyrThrGlyArgGlyIleArgProValGlyArgPhe    52

180 GGCAGGAGAAGGGCAACCCCGAGGGATGTCACTGGACTTGGCCAACTCAGCTGCCTCCCA   239
 53 GlyArgArgArgAlaThrProArgAspValThrGlyLeuGlyGlnLeuSerCysLeuPro    72

240 CTGGATGGACGCACCAAGTTCTCTCAGCGTGGATAACACCCCAGCTCGAGAAGACAGTGC   299
 73 LeuAspGlyArgThrLysPheSerGlnArgGly***                            83

300 TGCTGAGCCCAAGCCCACACTCCCTGTCCCCTGCAGACCCTCCTCTACCCTCCCTCTCCT   359
 83                                                                 83

360 CTGCT                                                          364
 83                                                                 83
```

09/446543

Fig. 33

```
bovine.aa                                  M  K  A   V  G  A   W  L  L
                        10         20         30         40         50
bovine.seq  -18 .......... ........GT GGAATGAAGG CGGTGGGGGC CTGGCTCCTC    32
rat.seq       1 GGCATCATCC AGGAAGACGG AGCATG---G CCCTGAAGAC GTGGCTTCTG    50

bovine.aa        C  L  L  L   L  G  L  A   L  Q   G  A  A  S   R  A  H
                        60         70         80         90        100
bovine.seq   33 TGCCTGCTGC TGCTGGGCCT GGCCCTGCAG GGGGCTGCCA GCAGAGCCCA    82
rat.seq      51 TGCTTGCTGC TGCTAAGCTT GGTCCTCCCA GGGGCTTCCA GCCGAGCCCA   100
                             R1

bovine.aa         Q  H  S   M  E  I  R   T  P  D   I  N  P   A  W  Y  A
                       110        120        130        140        150
bovine.seq   83 CCAGCACTCC ATGGAGATCC GCACCCCCGA CATCAACCCT GCCTGGTACG   132
rat.seq     101 CCAGCACTCC ATGGAGACAA GAACCCCTGA TATCAATCCT GCCTGGTACA   150
                                                              R3

bovine.aa         G  R  G   I  R  P   V  G  R  F   G  R  R   R  A  A
                       160        170        180        190        200
bovine.seq  133 CGGGCCGTGG GATCCGGCCC GTGGGCCGCT TCGGCCGGCG AAGAGCTGCC   182
rat.seq     151 CGGGCCGCGG GATCAGGCCT GTGGGCCGCT TCGGCAGGAG AAGGGCAACC   200
                                        R4

bovine.aa        P  G  D  G   P  R  P   G  P  R   R  V  P  A   C  F  R
                       210        220        230        240        250
bovine.seq  183 CCGGGGGACG GACCCAGGCC TGGCCCCCGG CGTGTGCCGG CCTGCTTCCG   232
rat.seq     201 CCGAGGGATG TCACTGGACT TGGC------ ---CAACTCA GCTGCCTCCC   250

bovine.aa         L  E  G   G  A  E  P   S  R  A   L  P  G  R   L  T  A
                       260        270        280        290        300
bovine.seq  233 CCTGGAAGGC GGCGCTGAGC CCTCCCGAGC CCTCCCGGGG CGGCTGACGG   282
rat.seq     251 ACTGGATGGA CGCACCAAGT TCTCTCAGCG TGGATAACAC CCCAGCTCGA   300

bovine.aa         Q  L  V   Q  E  *
                       310        320        330        340        350
bovine.seq  283 CCCAGCTGGT CCAGGAATAA CAGCGGGAGC CTGCCCCCCA CCCCTCCTCC   332
rat.seq     301 GAAGACAGTG CTGCTGAGCC CAAGCCCACA CTCCCTGTCC CCTGCAGACC   350

                       360        370        380        390        400
bovine.seq  333 TCCACCAGCC ACCTTCCCTC CAGTCCTAAT AAAAGCAGCT GGCTTGTT..   382
rat.seq     351 CTCCTCTACC CTCCCTCTCC TCTGCT.... .......... ..........   400
```

09/446543

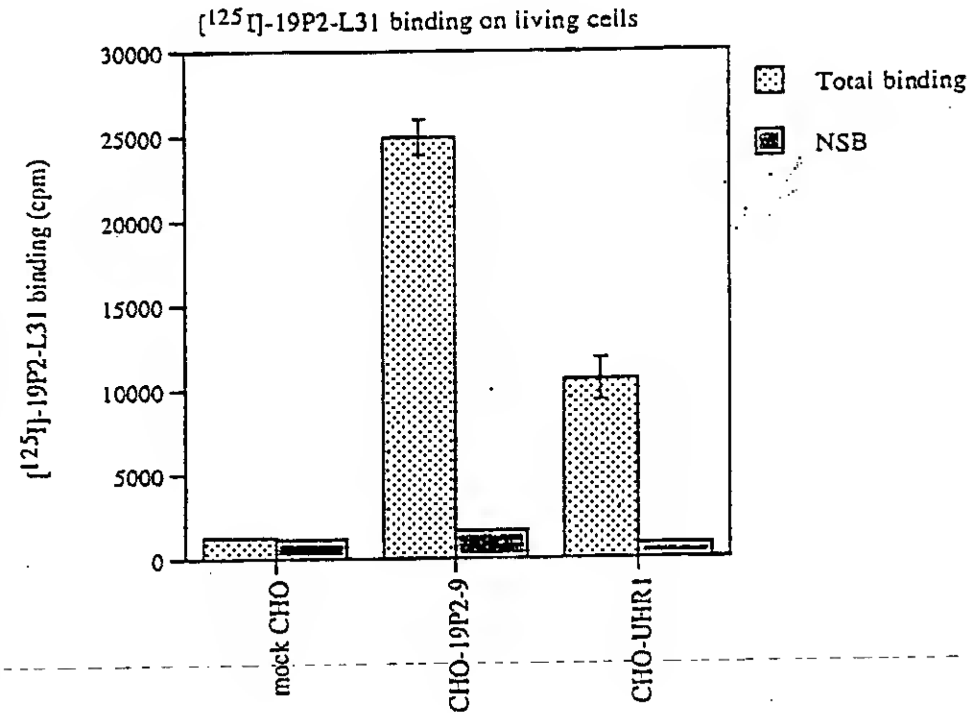
Fig. 34

1	GGCCTCCTCGGAGGAGCCAAGGGATGAAGGTGCTGAGGGCCTGGCTCCTGTGCCTGCTG	59
1	MetLysValLeuArgAlaTrpLeuLeuCysLeuLeu	12
60	ATGCTGGGCCTGGCCCTGCGGGGAGCTGCAAGTCGTACCCATCGGCACTCCATGGAGATC	119
13	MetLeuGlyLeuAlaLeuArgGlyAlaAlaSerArgThrHisArgHisSerMetGluIle	32
120	CGCACCCCTGACATCAATCCTGCCTGGTACGCCAGTCGCGGGATCAGGCCTGTGGGCCGC	179
33	ArgThrProAspIleAsnProAlaTrpTyrAlaSerArgGlyIleArgProValGlyArg	52
180	TTCGGTCGGAGGAGGGCAACCCTGGGGGACGTCCCCAAGCCTGGCCTGCGACCCCGGCTG	239
53	PheGlyArgArgArgAlaThrLeuGlyAspValProLysProGlyLeuArgProArgLeu	72
240	ACCTGCTTCCCCCTGGAAGGCGGTGCTATGTCGTCCCAGGATGGCTGACAGCCAGCTTGT	299
73	ThrCysPheProLeuGluGlyGlyAlaMetSerSerGlnAspGly***	87
300	CAAGAAACTCACTCTGGAGCCTCCCCCACCCCACCCTCTCCTCTCCTTCGGGCTCCTTTC	359
87		87
360	CC	361
87		87

Fig. 35

```
                          10         20         30         40         50
bovine.aa    1 MKAVGAWLLC LLLLGLALQG AASRAHQHSM EIRTPDINPA WYAGRGIRPV    50
rat.aa       1 M-ALKTWLLC LLLLSLVLPG ASSRAHQHSM ETRTPDINPA WYTGRGIRPV    50
human.aa     1 MKVLRAWLLC LLMLGLALRG AASRTHRHSM EIRTPDINPA WYASRGIRPV    50

                          60         70         80         90        100
bovine.aa   51 GRFGRRRAAP GDGPRPGPRR VPACFRLEGG AEPSRALPGR LTAQLVQE*.   100
rat.aa      51 GRFGRRRATP RDVTGLG--- QLSCLPLDGR TKFSQRG*.. ..........   100
human.aa    51 GRFGRRRATL GDVPKPGLRP RLTCFPLEGG AMSSQDG*.. ..........   100
```

Fig. 36



cells; 0.5 x 10^7 cells/ml
[^{125}I]-19P2-L31; 200pM(avg.63857.3cpm)
NSB; 200nM(x 1,000)
reaction; RT, 2.5hr
in HBSS + 0.05% BSA + 0.05% CHAPS
in 100 µl

Fig. 37

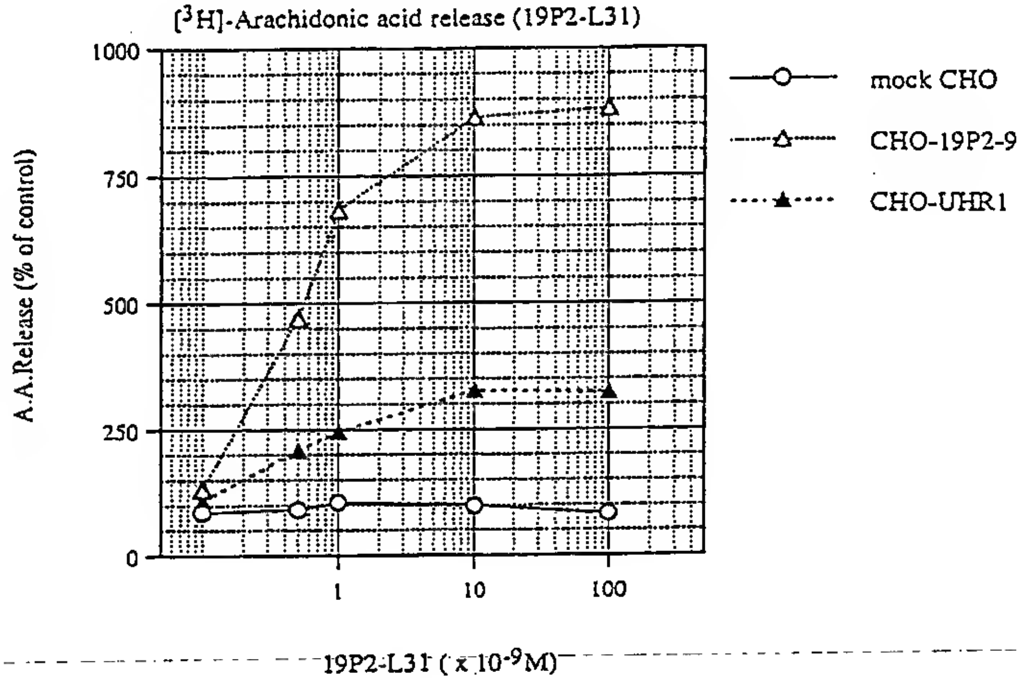
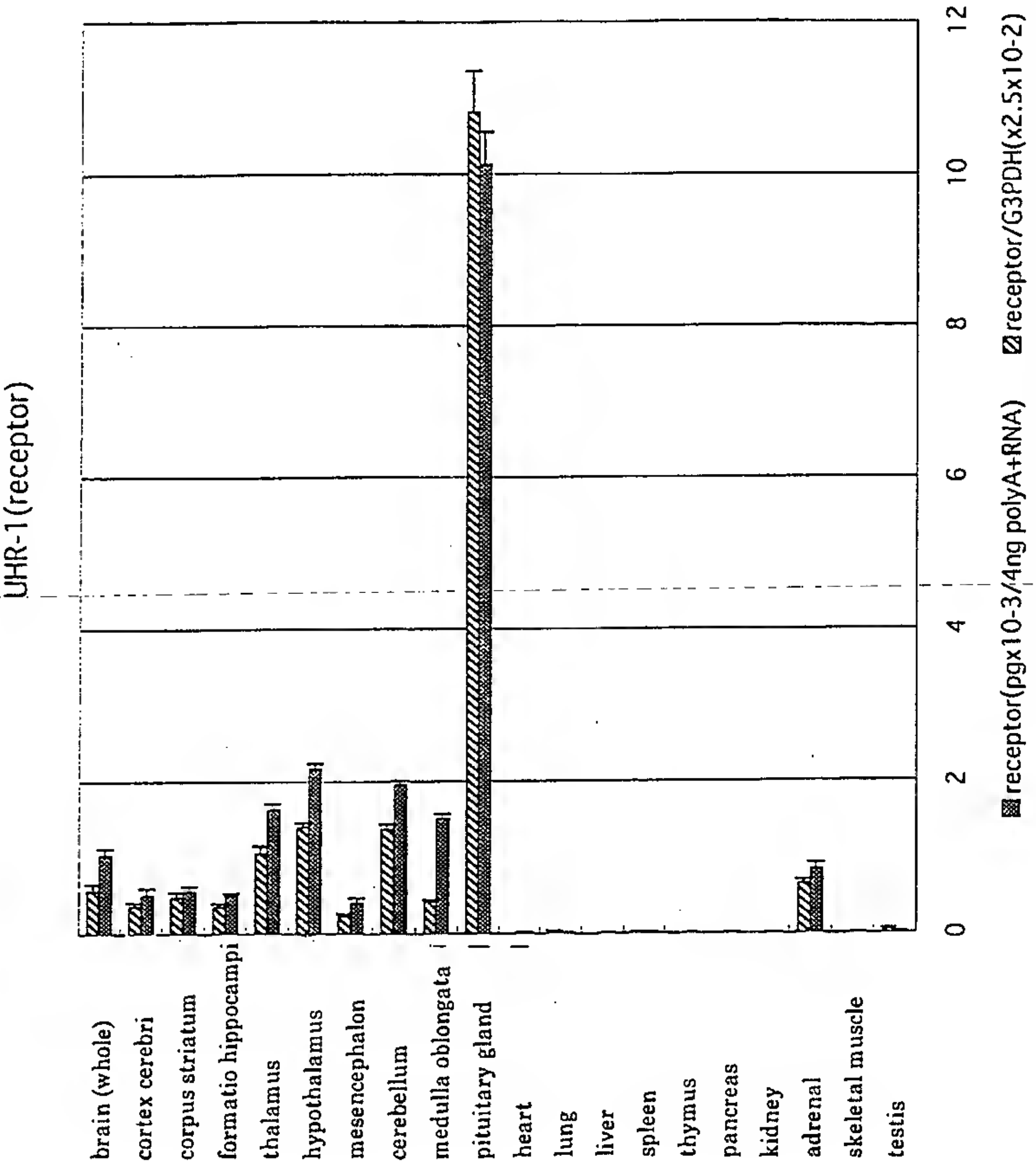

[3H]-Arachidonic acid release (19P2-L31)
A.A.Release (% of control)
1000
750
500
250
0
1
10
100
19P2-L31 (x 10-9M)
mock CHO
CHO-19P2-9
CHO-UHR1

Fig. 38



UHR-1(receptor)
0
2
4
6
8
10
12
receptor(pgx10-3/4ng polyA+RNA)
receptor/G3PDH(x2.5x10-2)
brain (whole)
cortex cerebri
corpus striatum
formatio hippocampi
thalamus
hypothalamus
mesencephalon
cerebellum
medulla oblongata
pituitary gland
heart
lung
liver
spleen
thymus
pancreas
kidney
adrenal
skeletal muscle
testis

Fig. 39

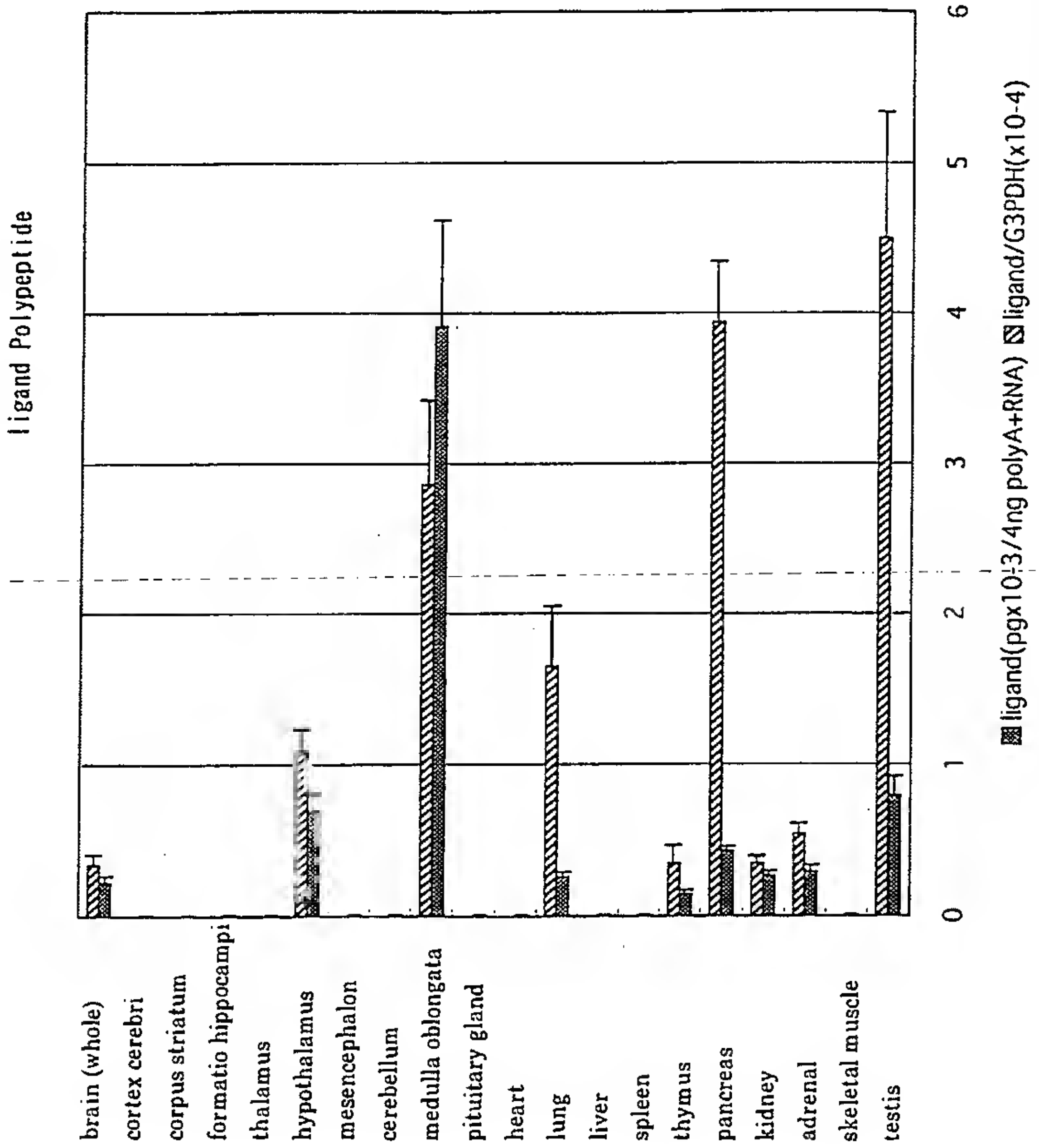
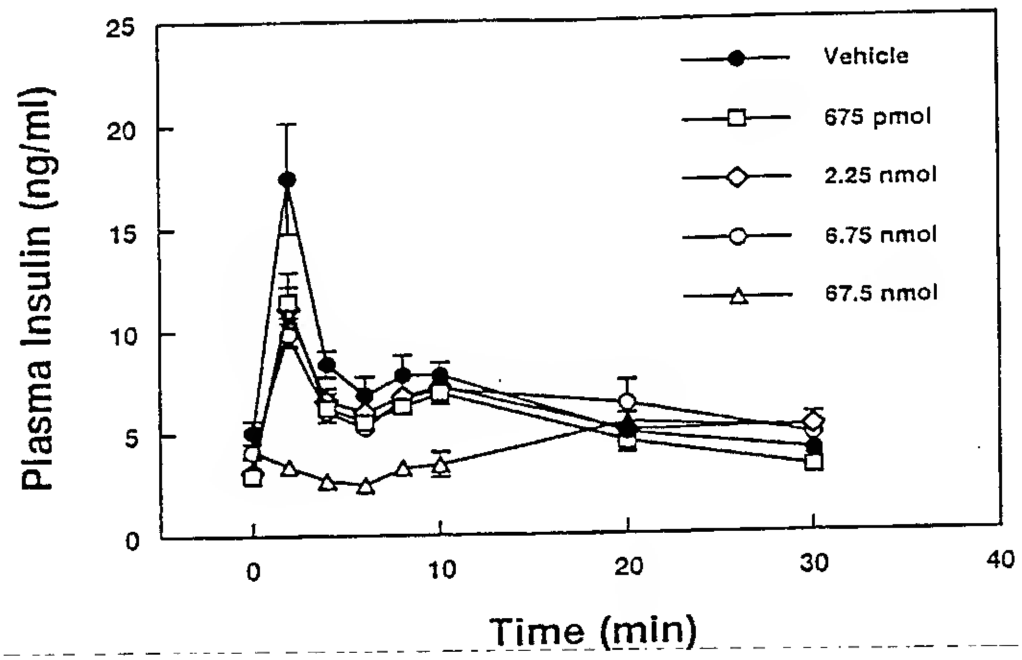

ligand Polypeptide
brain (whole)
cortex cerebri
corpus striatum
formatio hippocampi
thalamus
hypothalamus
mesencephalon
cerebellum
medulla oblongata
pituitary gland
heart
lung
liver
spleen
thymus
pancreas
kidney
adrenal
skeletal muscle
testis
0
1
2
3
4
5
6
ligand(pgx10-3/4ng polyA+RNA)
ligand/G3PDH(x10-4)

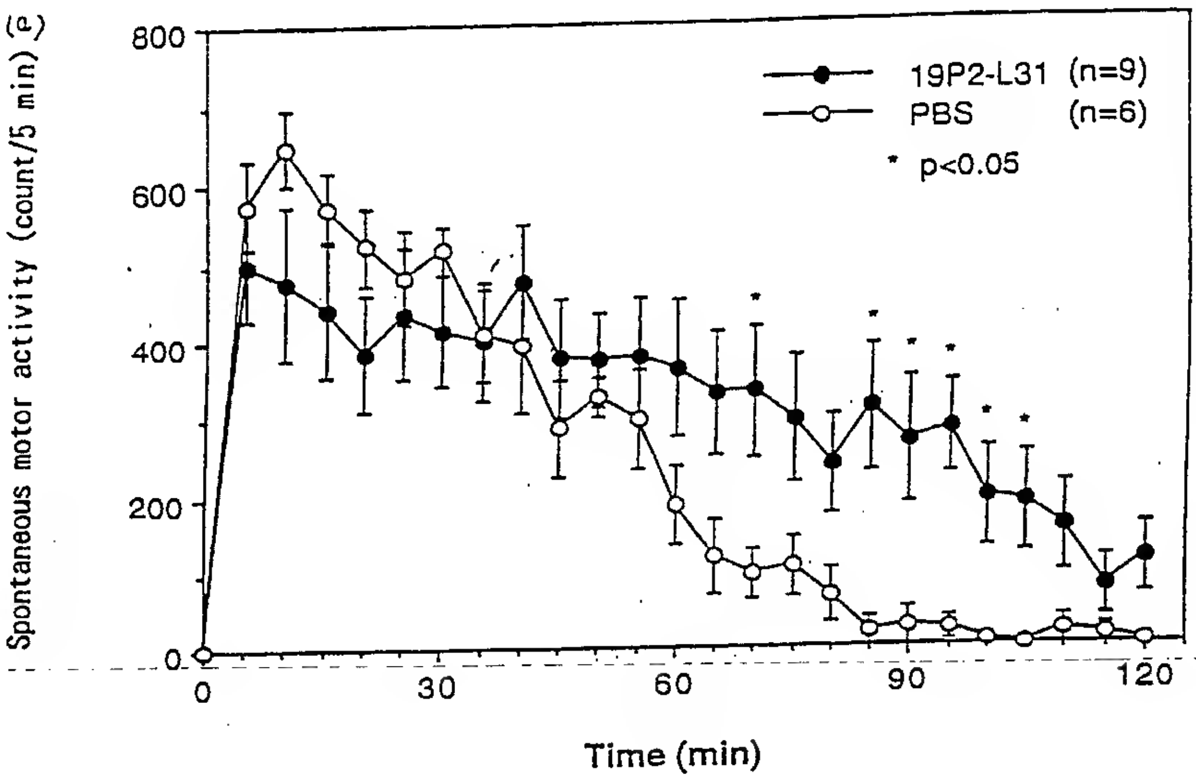
Fig. 40



Plasma Insulin (ng/ml)
25
20
15
10
5
0
0
10
20
30
40
Time (min)
Vehicle
675 pmol
2.25 nmol
6.75 nmol
67.5 nmol

Fig. 41

(a)


800
600
400
200
0
Spontaneous motor activity (count/5 min)
0
30
60
90
120
Time (min)
19P2-L31 (n=9)
PBS (n=6)
* p<0.05

(b)

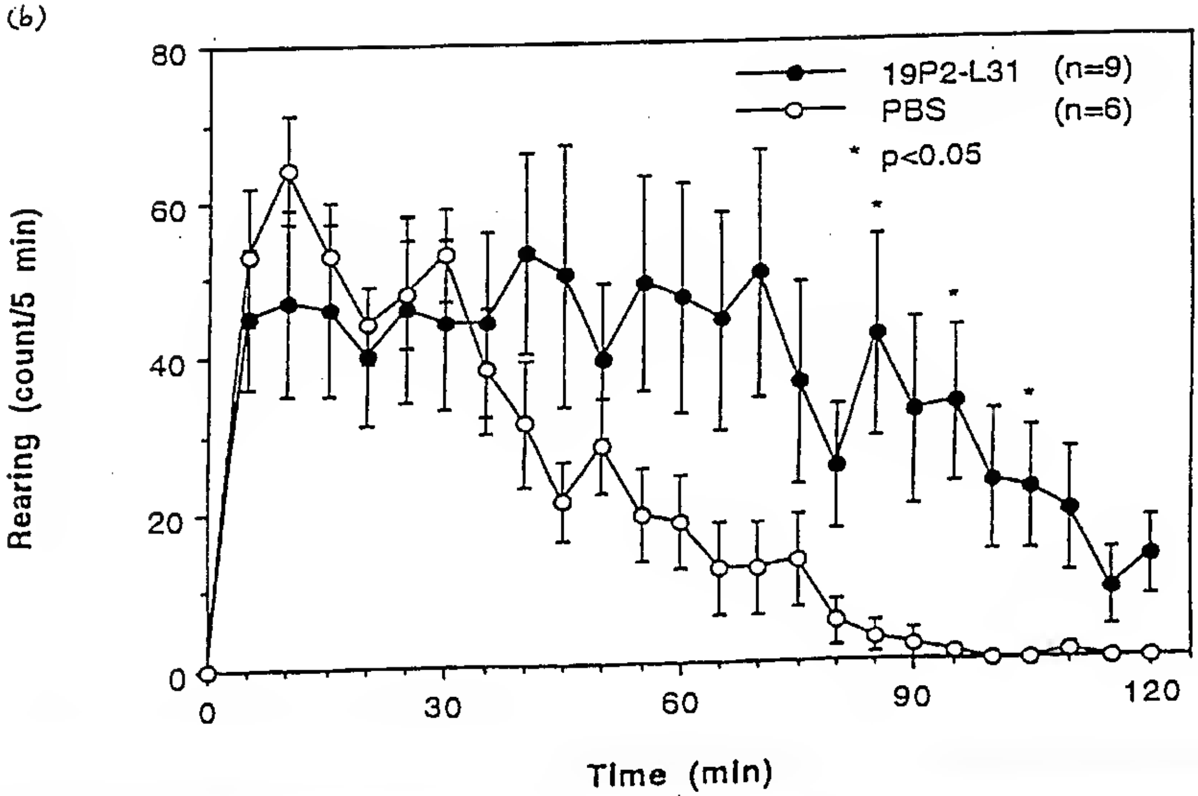
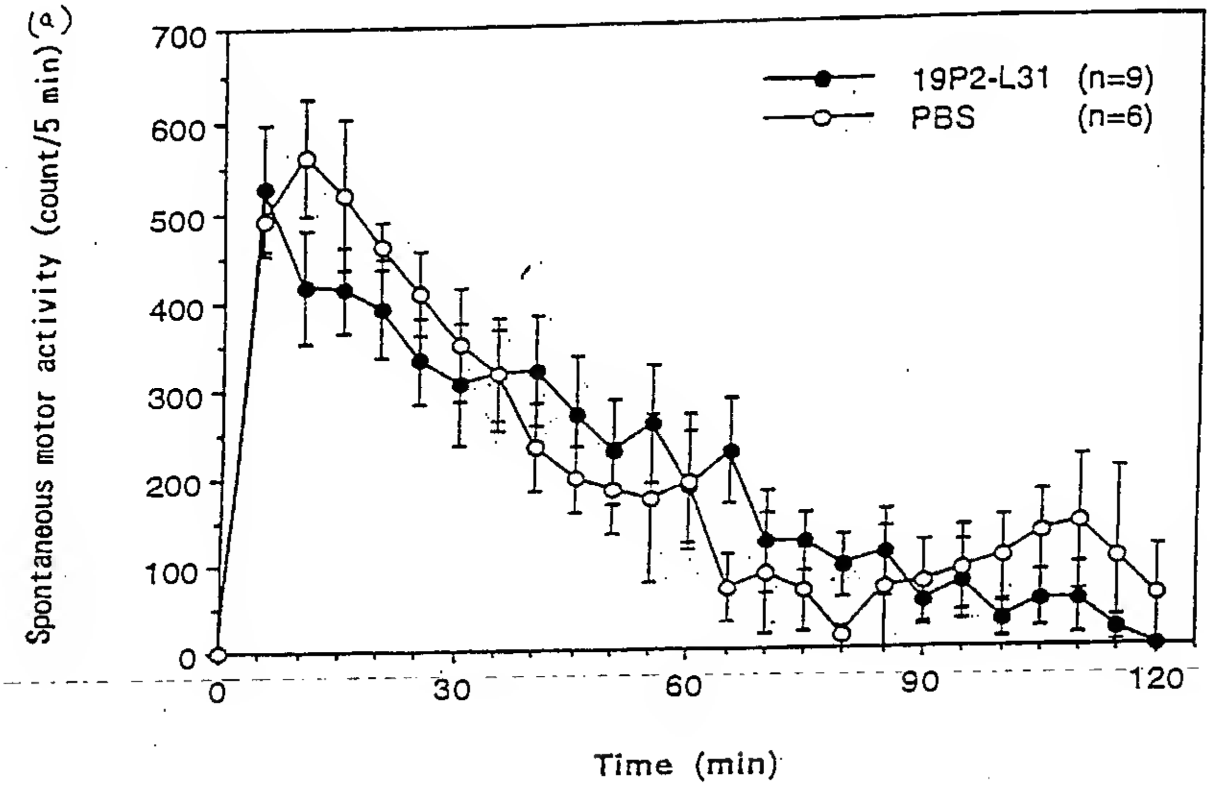

80
60
40
20
0
Rearing (count/5 min)
0
30
60
90
120
Time (min)
19P2-L31 (n=9)
PBS (n=6)
* p<0.05

Fig. 42

(a)


19P2-L31 (n=9)
PBS (n=6)
Spontaneous motor activity (count/5 min)
Time (min)
0
100
200
300
400
500
600
700
0
30
60
90
120

(b)

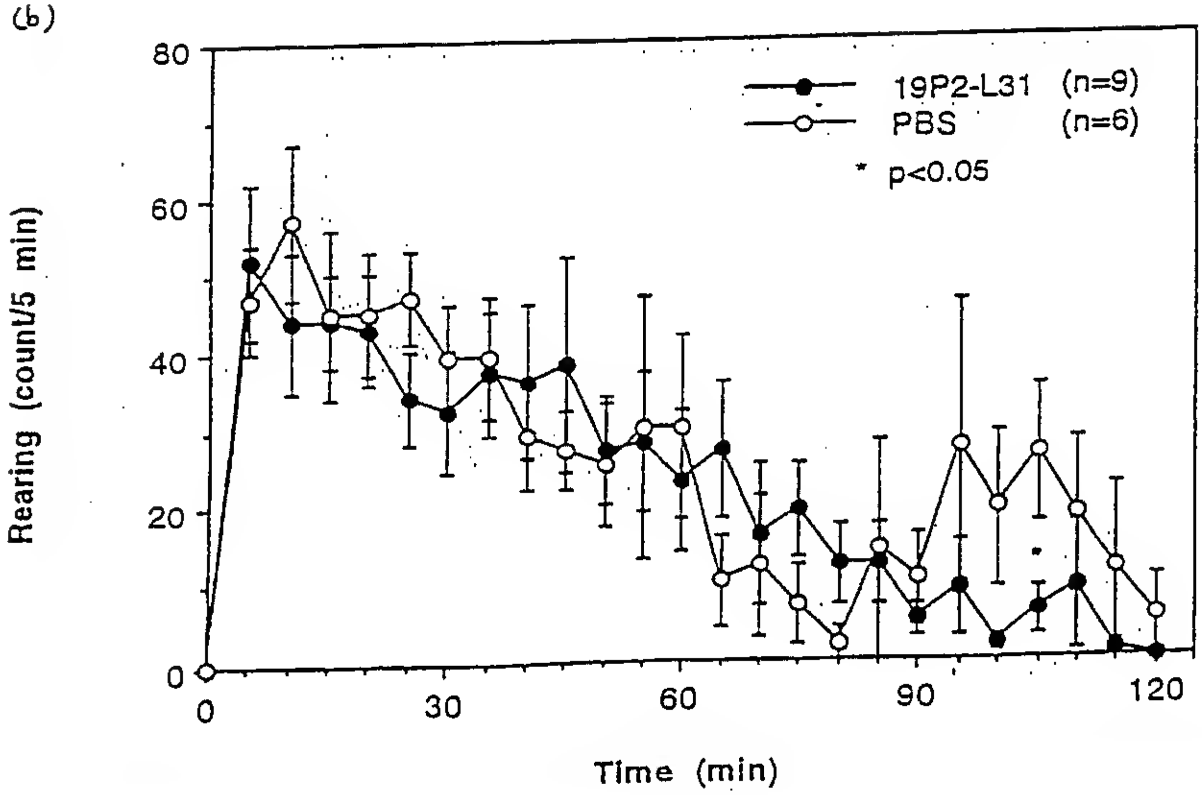
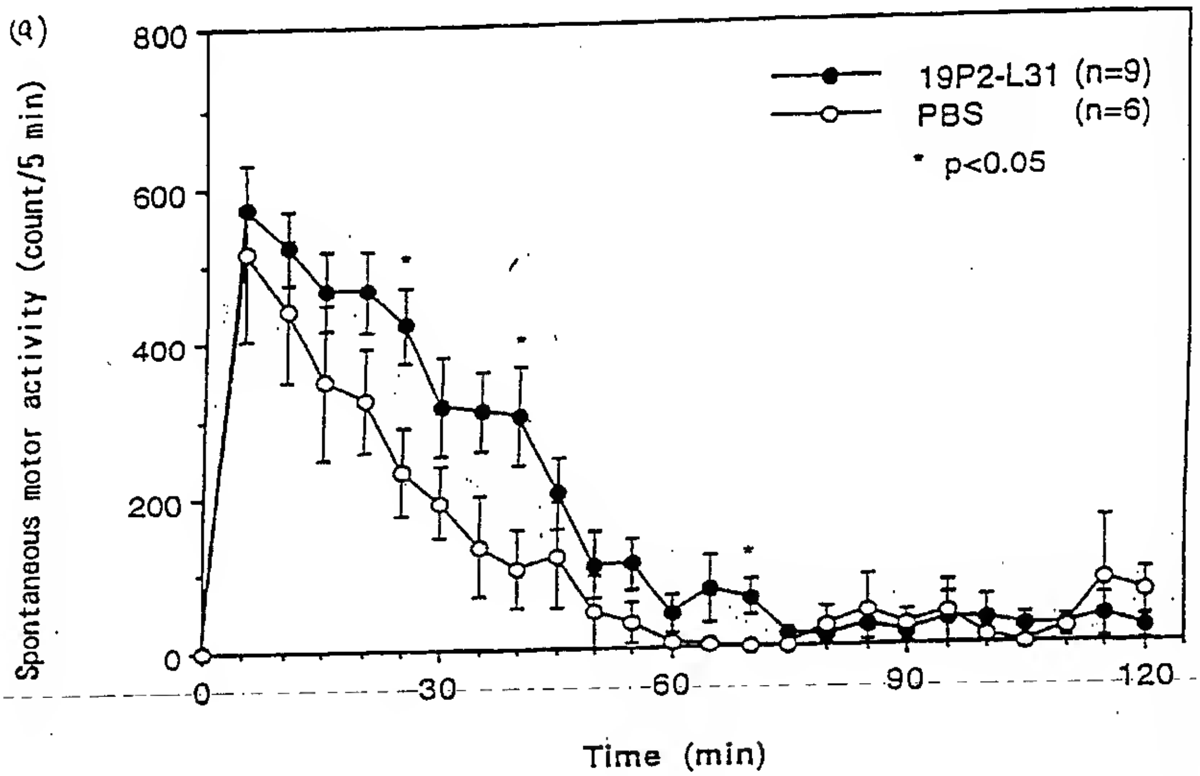

19P2-L31 (n=9)
PBS (n=6)
* p<0.05
Rearing (count/5 min)
Time (min)
0
20
40
60
80
0
30
60
90
120

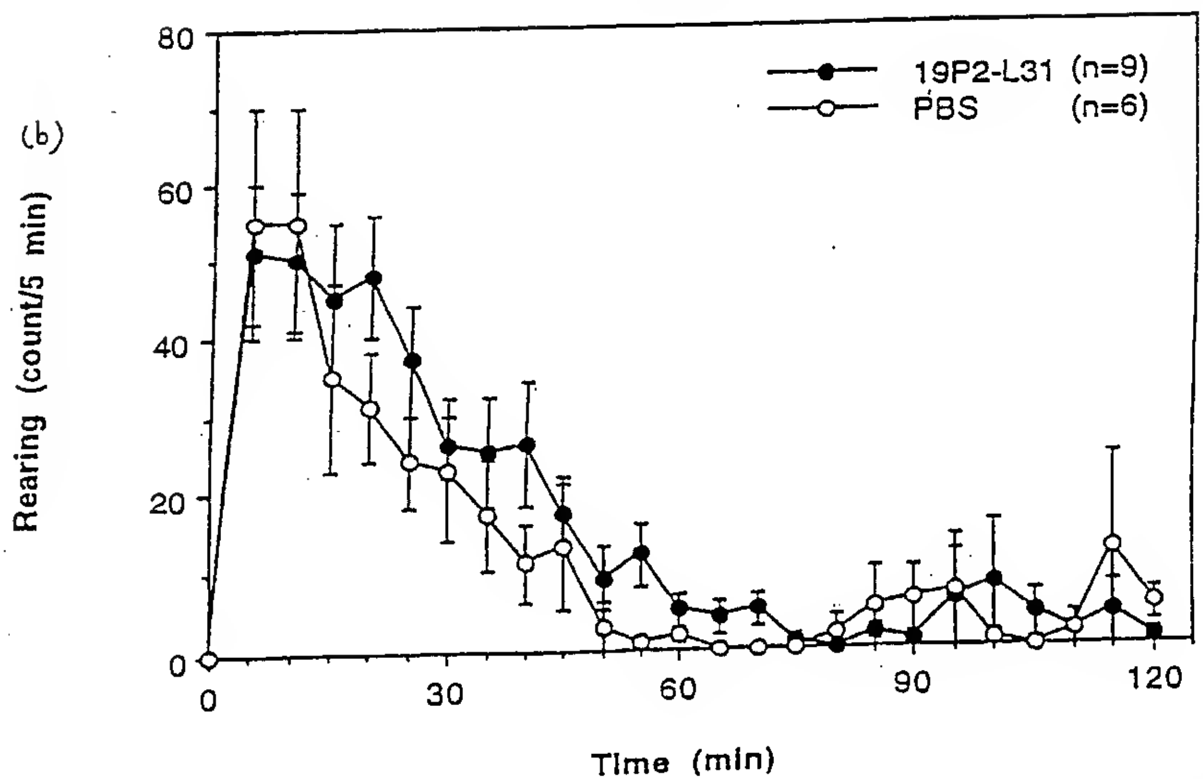
Fig. 43

(a)



800
600
400
200
0
Spontaneous motor activity (count/5 min)
19P2-L31 (n=9)
PBS (n=6)
* p<0.05
0
30
60
90
120
Time (min)

(b)

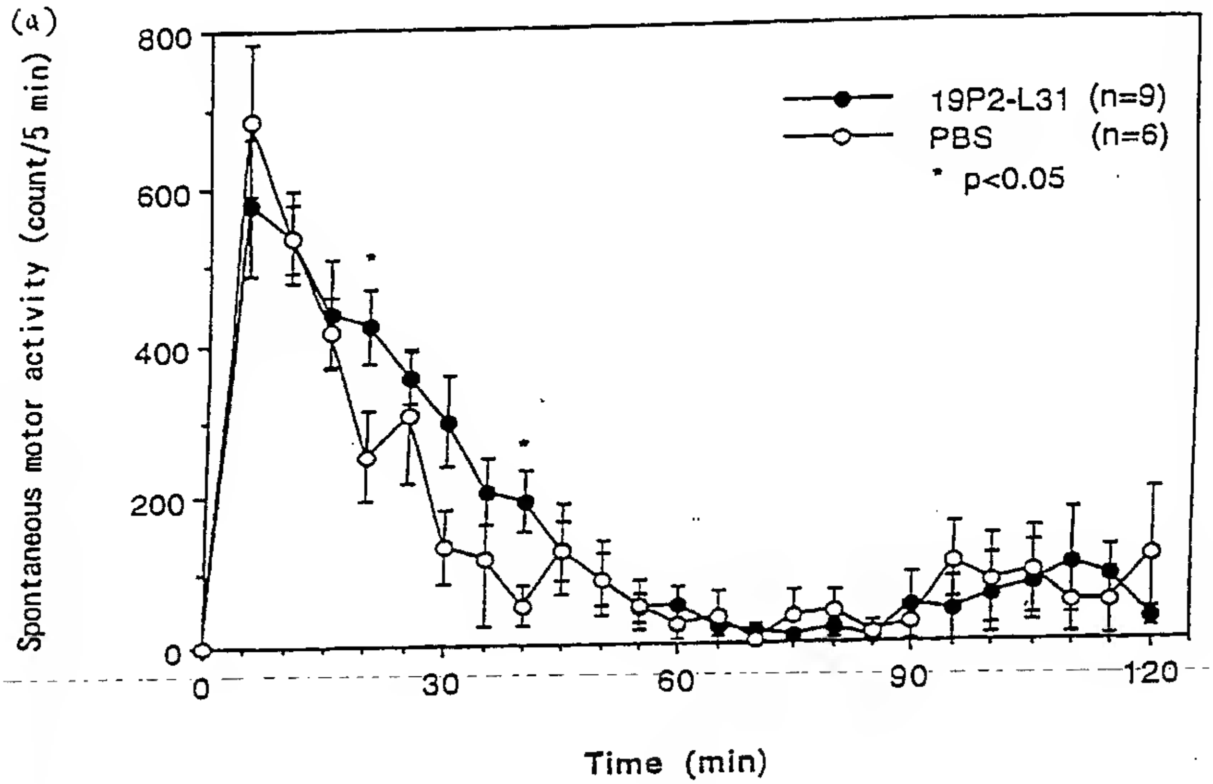


80
60
40
20
0
Rearing (count/5 min)
19P2-L31 (n=9)
PBS (n=6)
0
30
60
90
120
Time (min)

09/446543

Fig. 44

(a)



(b)

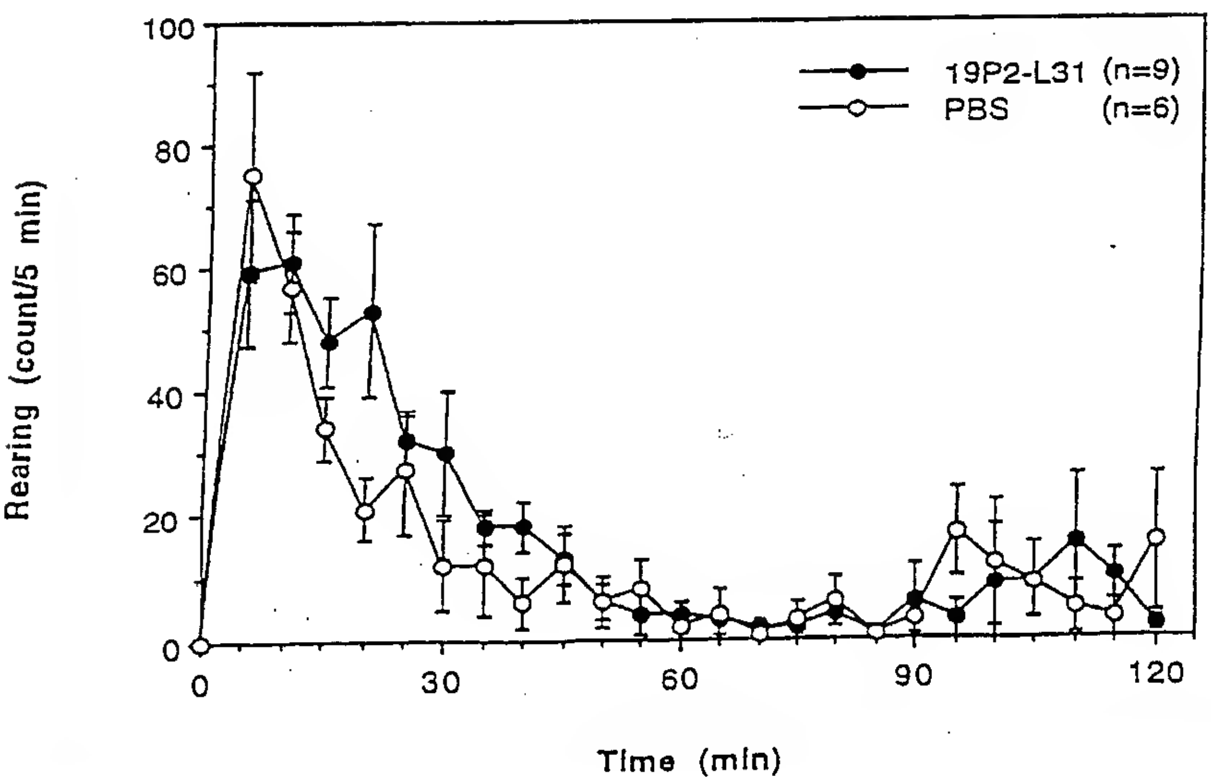
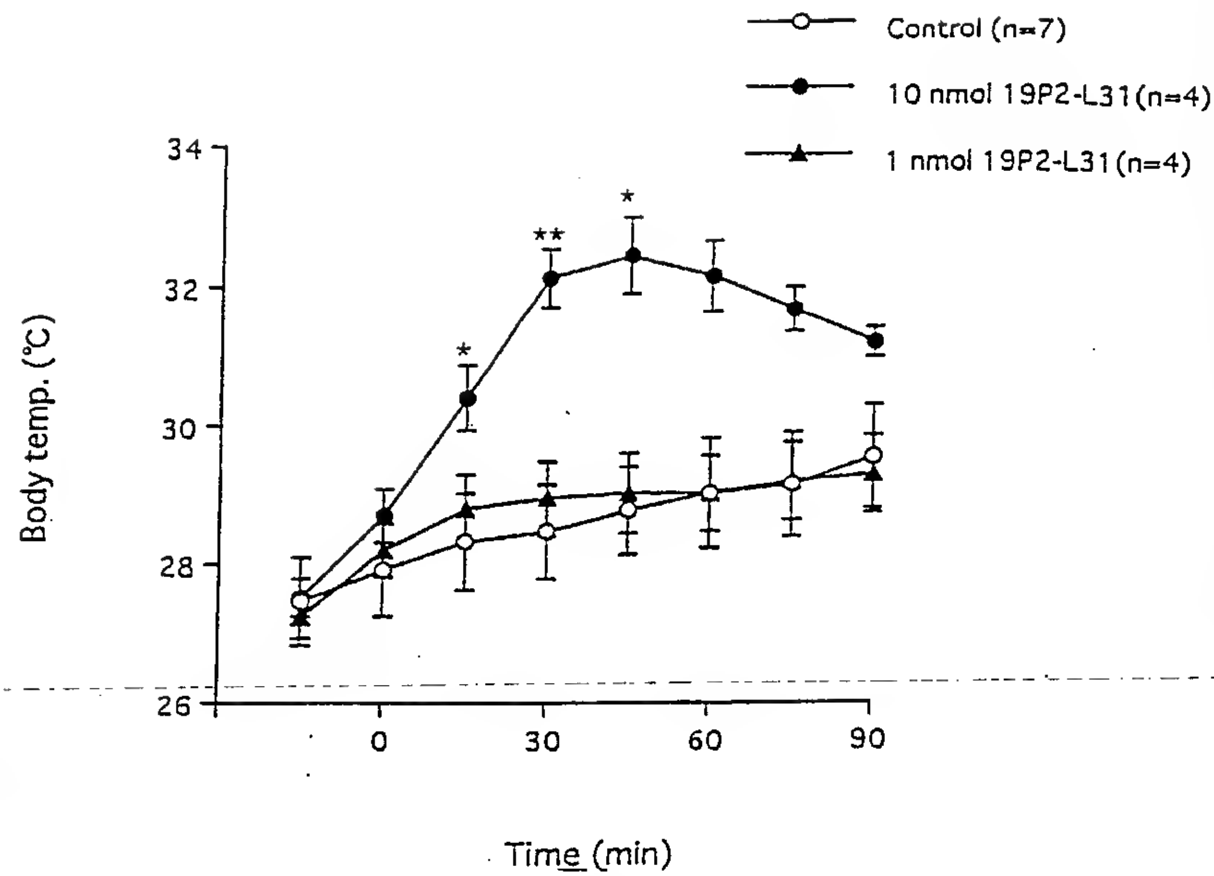


Fig. 45



Control (n=7)
10 nmol 19P2-L31(n=4)
1 nmol 19P2-L31(n=4)
Body temp. (°C)
34
32
30
28
26
*
**
*
0
30
60
90
Time (min)

Fig. 46

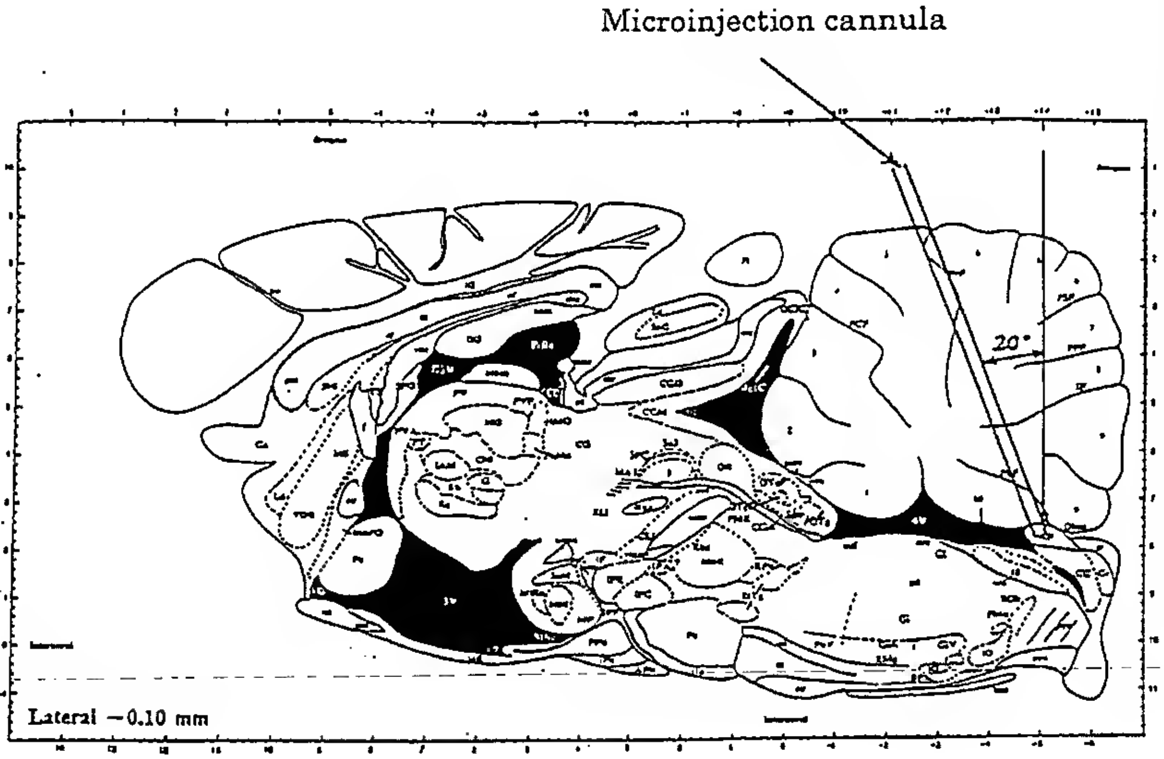


Fig. 47

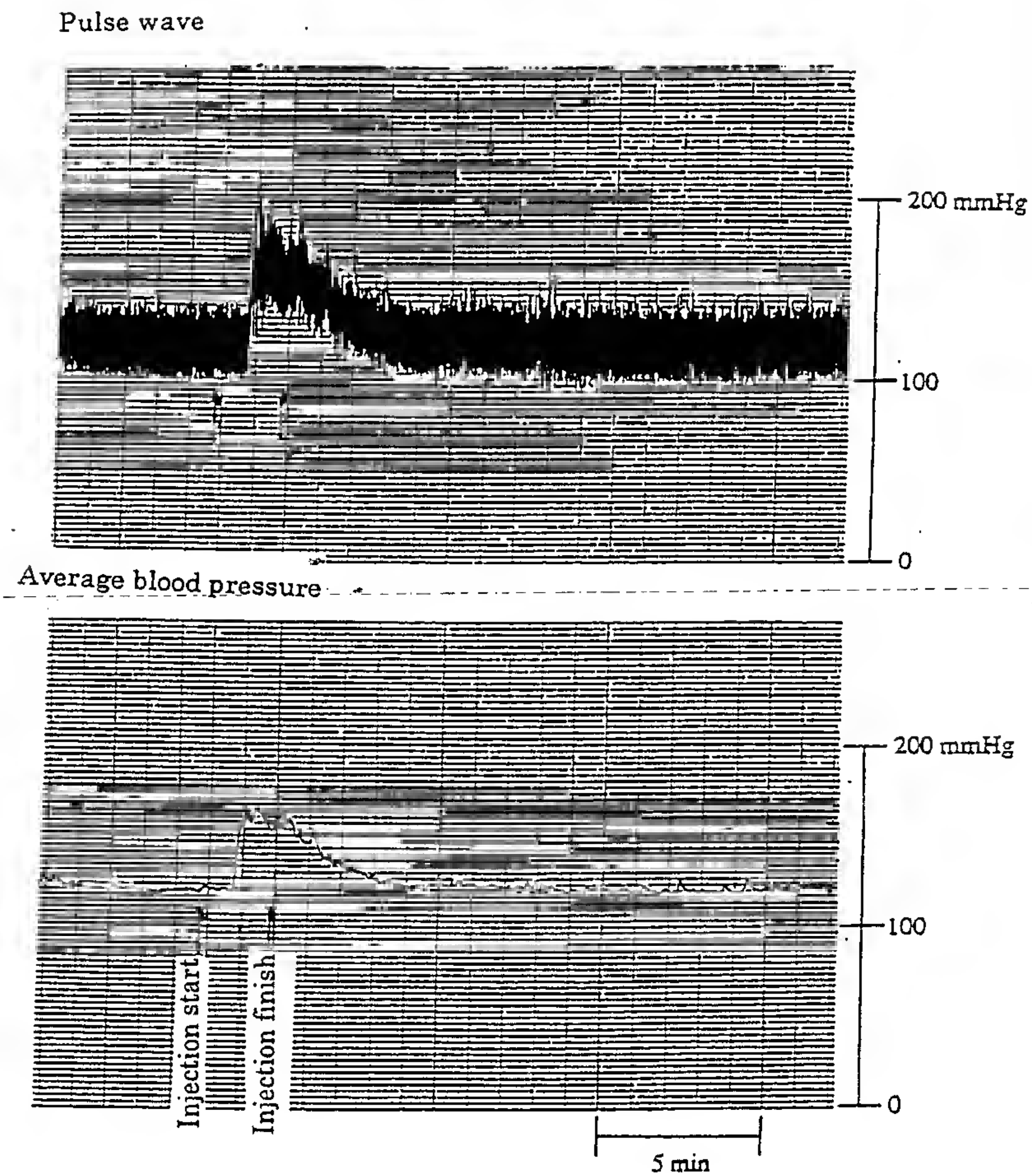

Pulse wave
200 mmHg
100
0
Average blood pressure
200 mmHg
100
0
Injection start
Injection finish
5 min

Fig. 48

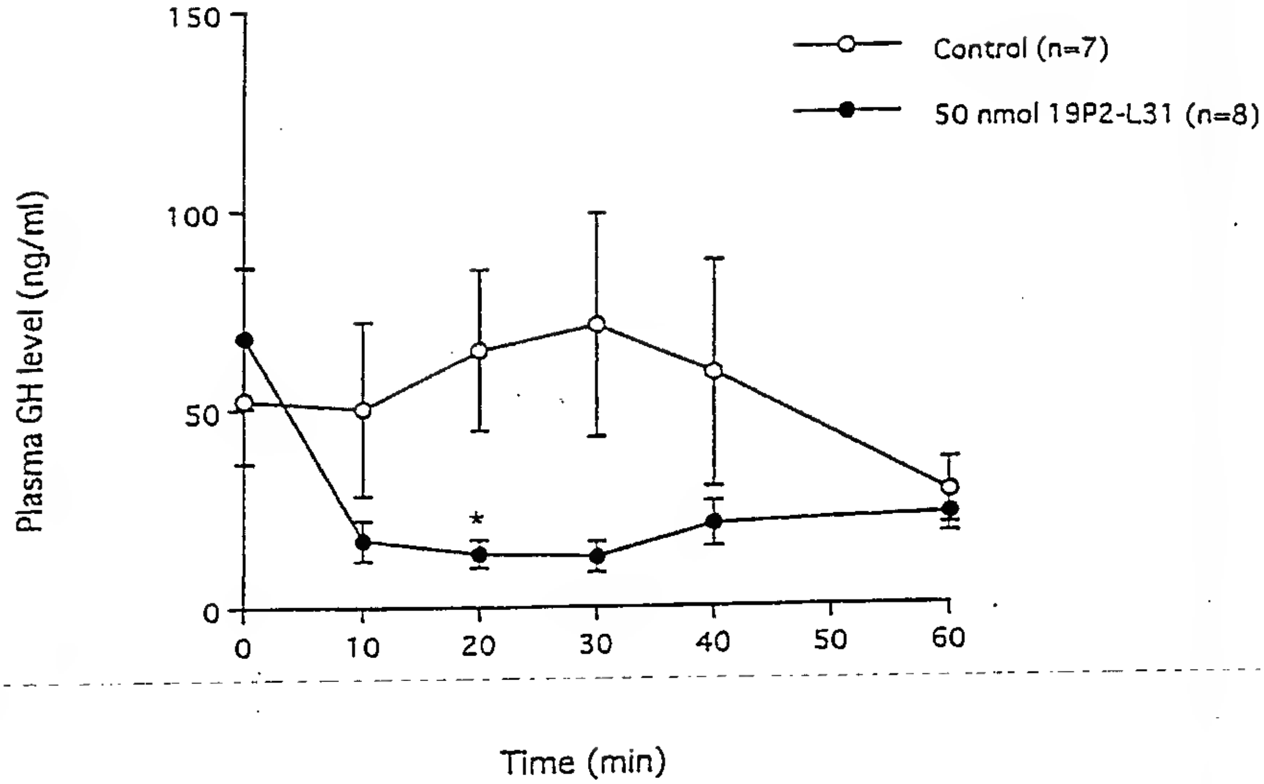
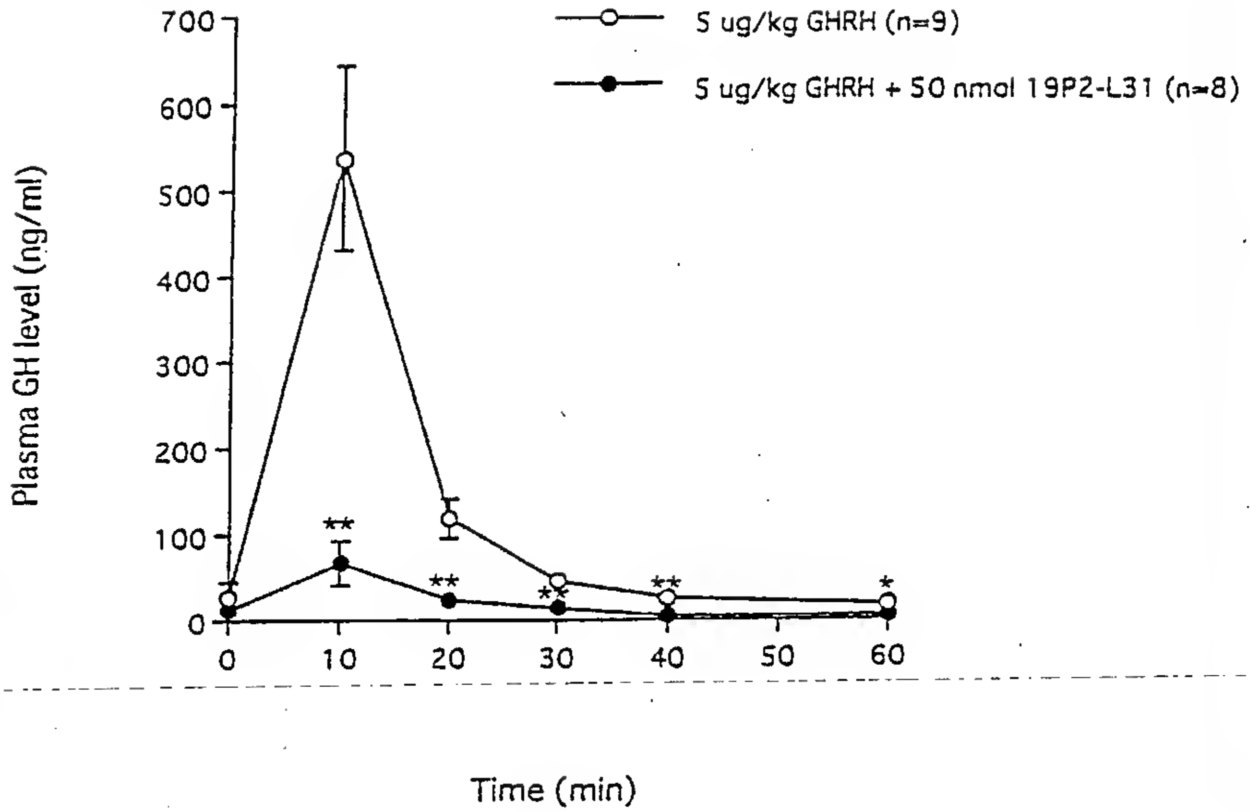

150
100
50
0
Plasma GH level (ng/ml)
0
10
20
30
40
50
60
Time (min)
Control (n=7)
50 nmol 19P2-L31 (n=8)
*

Fig. 49



5 ug/kg GHRH (n=9)
5 ug/kg GHRH + 50 nmol 19P2-L31 (n=8)
Plasma GH level (ng/ml)
700
600
500
400
300
200
100
0
**
**
**
**
*
0
10
20
30
40
50
60
Time (min)

09/446543

Fig. 50

Titeration curve of anti-bovine 19P2 peptide I, II III serum using HRP-peptide I, II or III

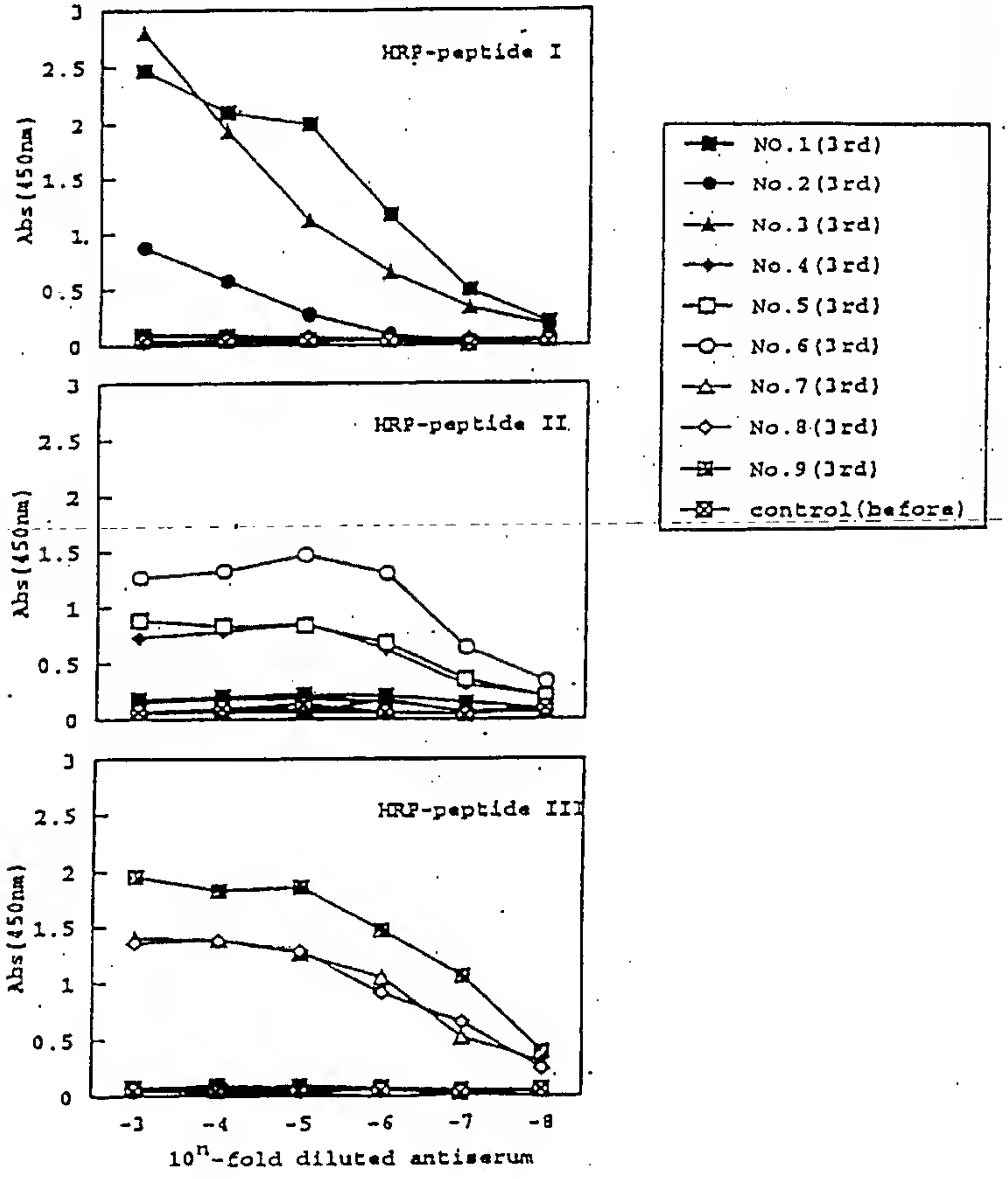
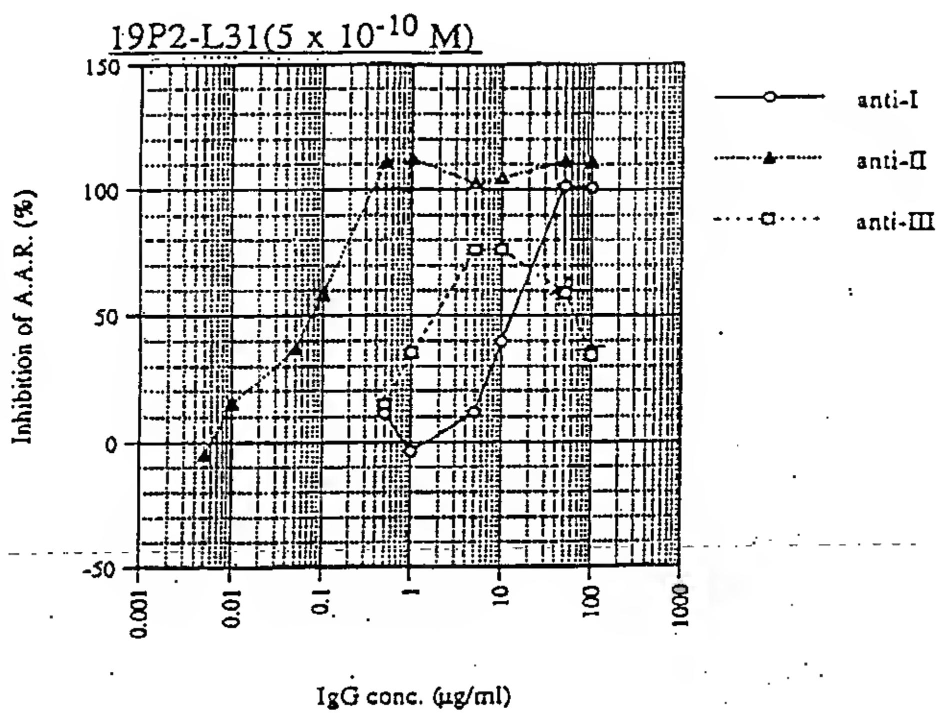


Fig. 51

Inhibition of A.A release by anti 19P2 peptide



09/446543

Fig. 52

```
                9           18          27          36          45          54
5' ATG ACC TCA CTG CCC CCT GGA ACC ACT GGG GAC CCC GAT TTC TTT TCT GGG CCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Met Thr Ser Leu Pro Pro Gly Thr Thr Gly Asp Pro Asp Leu Phe Ser Gly Pro

                63          72          81          90          99          108
   TCG CCA GCC GGC TCC ACT CCA GCC AAC CAC AGT GCA GAG GCT TCA GAG AGC AAT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Ser Pro Ale Gly Ser Thr Pro Ala Asn Gln Ser Ala Glu Ala Ser Glu Ser Asn

                117         126         135         144         153         162
   GTG TCT GCG ACC GTT CCC AGA GCT GCA GCA GTG ACG CCC TTC CAG AGC CTG CAA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Val Ser Ala Thr Val Pro Arg Ala Ala Ala Val Thr Pro Phe Gln Ser Leu Gln

                171         180         189         198         207         216
   CTA GTG CAC CAG CTG AAG GGA CTG ATC GTG ATG CTG TAC AGC ATC GTG GTG GTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu Val His Gln Leu Lys Gly Leu Ila Val Met Leu Tyr Ser Ile Val Val Val

                225         234         243         252         261         270
   GTG GGT CTC GTG GGC AAC TGC CTT CTT GTG CTG GTG ATC GCG CGC GTG CGC CGG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Val Gly Leu Val Gly Asn Cys Leu Leu Val Leu Val Ile Ala Arg Val Arg Arg

                279         288         297         306         315         324
   CTC CAC AAC GTG ACC AAC TTC CTC ATC GGC AAC CTC GCC TTG TCC GAT GTG CTC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu His Asn Val Thr Asn Phe Leu Ile Gly Asn Leu Ala Leu Ser Asp Val Leu

                333         342         351         360         369         378
   ATG TGT GCC GCC TGT GTG CCT CTC ACG CTG GCC TAC GCC TTT GAA CCT CGT GGC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Met Cys Ala Ala Cys Val Pro Leu Thr Leu Ala Tyr Ala Phe Glu Pro Arg Gly

                387         396         405         414         423         432
   TGG GTG TTC GGT GGA GGC CTC TGC CAC CTT GTT TTC TTC CTG CAG CCG GTG ACC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Trp Val Phe Gly Gly Gly Leu Cys His Leu Val Phe Phe Leu Gln Pro Val Thr

                441         450         459         468         477         486
   GTC TAC GTA TCG GTG TTC ACA CTC ACC ACA ATC GCT GTG GAC CGC TAT GTG GTT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Val Tyr Val Ser Val Phe Thr Leu Thr Thr Ile Ala Val Asp Arg Tyr Val Val

                495         504         513         522         531         540
   CTC GTG CAC CCG CTA CGT CGC CGC ATT TCA CTC AAG CTG AGC GCG TAC GCC GTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu Val His Pro Leu Arg Arg Arg Ile Ser Leu Lys Leu Ser Ala Tyr Ala Val

                549         558         567         576         585         594
   CTG GGC ATC TGG GCT CTA TCT GCA GTG CTG GCC CTG CCG GCC GCC GTG CAC ACC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu Gly Ile Trp Ala Leu Ser Ala Val Leu Ala Leu Pro Ala Ala Val His Thr

                603         612         621         630         639         648
   TAC CAT GTA GAG CTG AAG CCG CAC GAC GTG CGC CTC TGC GAG GAG TTC TGG GGT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Tyr His Val Glu Leu Lys Pro His Asp Val Arg Leu Cys Glu Glu Phe Trp Gly

                657         666         675         684         693         702
   TCG CAG GAG CGC CAG CGA CAG ATC TAT GCC TGG GGG CTG CTC CTG GGC ACC TAT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Ser Gln Glu Arg Gln Arg Gln Ile Tyr Ala Trp Gly Leu Leu Leu Gly Thr Tyr

                711         720         729         738         747         756
   TTG CTG CCC CTC CTG GCC ATT CTG CTG TCT TAC GTC CGG GTG TCG GTG AAG TTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Leu Leu Pro Leu Leu Ala Ile Leu Leu Ser Tyr Val Arg Val Ser Val Lys Leu

                765         774         783         792         801         810
   CGC AAC CGC GTG GTG CCT GGC AGC GTG ACC CAG AGC CAG GCT GAC TGG GAC CGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Arg Asn Arg Val Val Pro Gly Ser Val Thr Gln Ser Gln Ala Asp Trp Asp Arg

                819         828         837         846         855         864
   GCC CGT CGC CGT CGC ACT TTC TGC CTG CTG GTG GTG GTG GTG GTG GTG TTC GCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Ala Arg Arg Arg Arg Thr Phe Cys Leu Leu Val Val Val Val Val Val Phe Ala

                873         882         891         900         909         918
   GTC TGC TGG CTG CCT CTG CAC ATT TTC AAC CTG CTG CGG GAC CTG GAC CCG CGT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Val Cys Trp Leu Pro Leu Hie Ile Phe Asn Leu Leu Arg Asp Leu Asp Pro Arg

                927         936         945         954         963         972
   GCC ATC GAC CCC TAC GCC TTC GGC CTG GTG CAG CTG CTG TGC CAC TGG CTT GCC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Ala Ile Asp Pro Tyr Ala Phe Gly Leu Val Gln Leu Leu Cys His Trp Leu Ala

                981         990         999         1008        1017        1026
   ATG AGC TCC GCC TGC TAC AAC CCC TTC ATC TAT GCC TGG CTG CAC GAC AGC TTC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Met Ser Ser Ale Cys Tyr Asn Pro Phe Ile Tyr Ala Trp Leu His Asp Ser Phe

                1035        1044        1053        1062        1071        1060
   CGA GAG GAG CTA CGC AAG ATG CTT CTG TCT TGG CCC CGC AAG ATC GTG CCT CAT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
   Arg Glu Glu Leu Arg Lys Met Leu Leu Ser Trp Pro Arg Lys Ile Val Pro His

                1089        1098        1107        1116
   GGC CAG AAT ATG ACC GTC AGT GTG GTC ATC TGA TGA 3'
   --- --- --- --- --- --- --- --- --- --- --- ---
   Gly Gln Asn Met Thr Val Ser Val Val Ile *** ***
```

09/446543

Fig. 53

10	20	30	40	50	60
AGATCTGGCA	TCATCCAGGA	AGACGGAGCA	TGGCACCGAG	GACCTGGCTT	CTGTGCTTGC
70	80	90	100	110	120
TGCTGCTAGG	CTTAGTCCTC	CCAGGAGCTT	CCAGCCGAGC	CCACCAGCAC	TCCATGGAGA
130	140	150	160	170	180
CCCGCAGTGA	GTGCCTGGCA	TATGGAGGAC	AGCCACTGTC	ACCTCCCATC	CATATGCTTC
190	200	210	220	230	240
CCAAATGCCT	TGAGTACCCA	GCCCCTGAAT	GGGAGGTTAG	CCATCTCCTA	AGCCAGTGGT
250	260	270	280	290	300
TTCCAACCTT	CCTAATACAG	AACTTTTAAT	ACAGATCCTT	ATGTTGTGGT	GACCCCCAGC
310	320	330	340	350	360
CAGAAAATTA	TTGTGATGCT	GTTTTCATAG	TTGTAAGTTT	TGCTACTGTT	ATGGATCATA
370	380	390	400	410	420
ATGTTAATAT	CTGAAATGCA	GGATGTCTGA	TATGCGCCCT	TCCCCCCAAA	CAAAAGGGAC
430	440	450	460	470	480
ACAACCCACA	GGTTGAGAGC	CTCTGGGATC	TAAGCAAAAG	CTACCTTACC	ATGCAGTCAG
490	500	510	520	530	540
TTGGGAGATT	GGTCCTGTTA	AGATCTCCCC	AGAATGGTCC	TGTTTCCTGT	CCTCATCATT
550	560	570	580	590	600
CCCCTAACCC	ATCTTTGTGG	GGTCCCTTAA	GACTTTGGAG	GATGACAGTC	AGACAGGAAG
610	620	630	640	650	660
AGAATACTGA	TCCTGGCATA	TGTCTAAATA	AATTCCCTAA	AGCCACACCA	CTGCCCAGAT
670	680	690	700	710	720
ATGCCCAGCC	AGTGTAATCA	GGGTGGGTGC	CAACATGGCC	TGGTGCCCAG	GTTTCCATCA
730	740	750	760	770	780
GCTTAGGGGC	TCCCGTGTCC	CATACGCTGC	TCTGACTCTT	TCCTTTCCAG	CCCCTGACAT
790	800	810	820	830	840
CAATCCTGCC	TGGTACACGG	GTCGTGGGAT	CAGGCCTGTG	GGCCGCTTCG	GGAGGAGGAG
850	860	870	880	890	900
GGCAGCCCTG	AGGGATGTCA	CCGGACCTGG	CCTGCGGTGC	CGGCTAAGCT	GCTTCCCACT
910	920	930	940	950	960
GGATGGAAGT	GCCAAGTTCT	CTCACAGCTC	GAGAAGACAG	TGCTGCTGAG	TCGAC....

Fig. 54

AG ATC TGG CAT CAT CCA GGA AGA CGG AGC ATG GCA CCG AGG ACC TGG CTT CTG TGC
Met Ala Pro Arg Thr Trp Leu Leu Cys

TTG CTG CTG CTA GGC TTA GTC CTC CCA GGA GCT TCC AGC CGA GCC CAC CAG CAC
Leu Leu Leu Leu Gly Leu Val Leu Pro Gly Ala Ser Ser Arg Ala His Gln His

TCC ATG GAG ACC CGC A GT CAG TGC CTG GCA TAT GGA GGA CAG CCA CTG TCA CCT
Ser Met Glu Thr Arg

CCC ATC CAT ATG CTT CCC AAA TGC CTT GAG TAC CCA GCC CCT GAA TGG GAG GTT

AGC CAT CTC CTA AGC CAG TGG TTT CCA ACC TTC CTA ATA CAG AAC TTT TAA TAC

AGA TCC TTA TGT TGT GGT GAC CCC CAG CCA GAA AAT TAT TGT GAT GCT GTT TTC

ATA GTT GTA AGT TTT GCT ACT GTT ATG GAT CAT AAT GTT AAT ATC TGA AAT GCA

GGA TGT CTG ATA TGC GCC CTT CCC CCC AAA CAA AAG GGA CAC AAC CCA CAG GTT

CAG AGC CTC TGG GAT CTA AGC AAA AGC TAC CTT ACC ATG CAG TCA GTT GGG AGA

TTG GTC CTG TTA AGA TCT CCC CAG AAT GGT CCT GTT TCC TGT CCT CAT CAT TCC

CCT AAC CCA TCT TTG TGG GGT CCC TTA AGA CTT TGG AGG ATG ACA GTC AGA CAG

GAA CAG AAT ACT GAT CCT GGC ATA TGT CTA AAT AAA TTC CCT AAA GCC ACA CCA

CTG CCC AGA TAT GCC CAG CCA GTG TAA TCA GGG TGG GTG CCA ACA TGG CCT GGT

GCC CAG GTT TCC ATC AGC TTA GGG GCT CCC GTG TCC CAT ACG CTG CTC TGA CTC

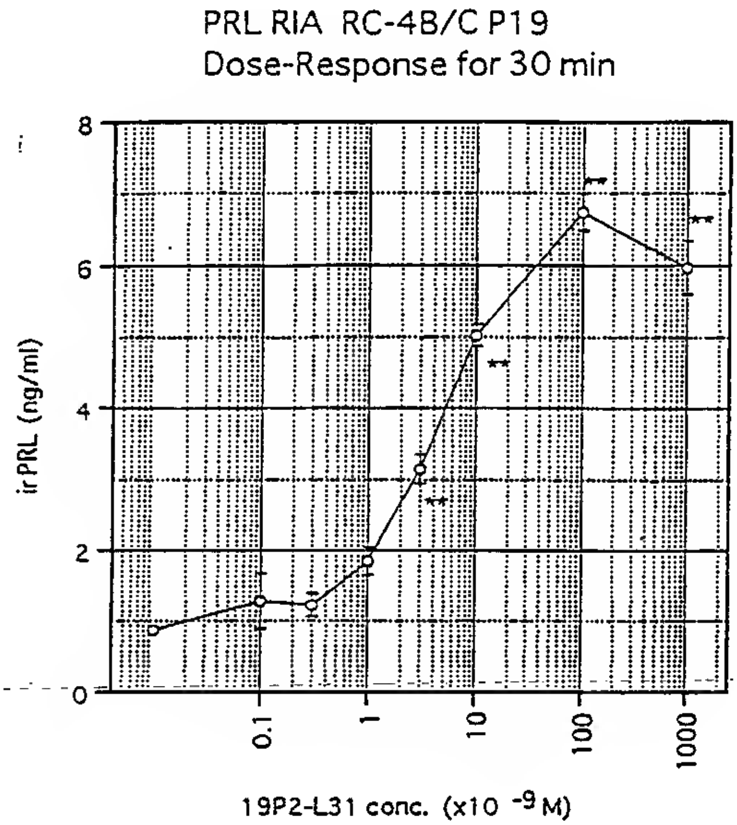
TTT CCT TTC CAG CC CCT GAC ATC AAT CCT GCC TGG TAC ACG GGT CGT GGG ATC
Thr Pro Asp Ile Asn Pro Ala Trp Tyr Thr Gly Arg Gly Ile

AGG CCT GTG GGC CGC TTC GGG AGG AGG AGG GCA GCC CTG AGG GAT GTC ACC GGA
Arg Pro Val Gly Arg Phe Gly Arg Arg Arg Ala Ala Leu Arg Asp Val Thr Gly

CCT GGC CTG CGG TGC CGG CTA AGC TGC TTC CCA CTG GAT GGA AGT GCC AAG TTC
Pro Gly Leu Arg Cys Arg Leu Ser Cys Phe Pro Leu Asp Gly Ser Ala Lys Phe

TCT CAG AGC TCG AGA AGA CAG TGC TGC TGA GTC GAC
Ser His Ser Ser Arg Arg Gln Cys Cys ***

Fig. 55



Cell Culture:RC-4B/C P19
1x10 5/well, for 2 Days
(12 well-plates)
(control: n=2, other points: n=4)

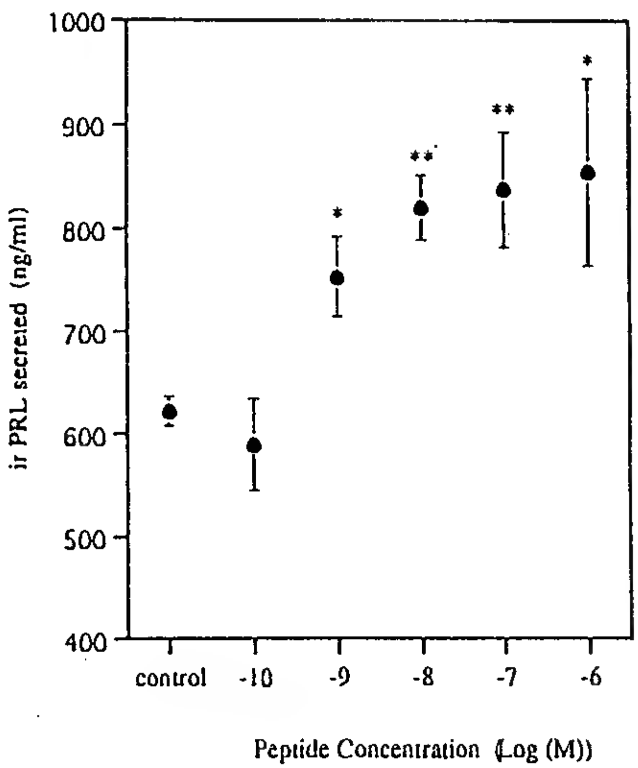
Wash 3 times
Pre-Incubation (for 15 min)
Wash twice, Add Samples
Incubation (for 30min)
Sup. Collected, Centrifuged

Assay: Rat [125I] Prolactin
Assay System (RIA) (Amersham)

**: p<0.01 (students' t-test)

Fig. 56

Effect of bovine 19P2-L31 Peptides
on PRL Secretion from Pituitary Cells



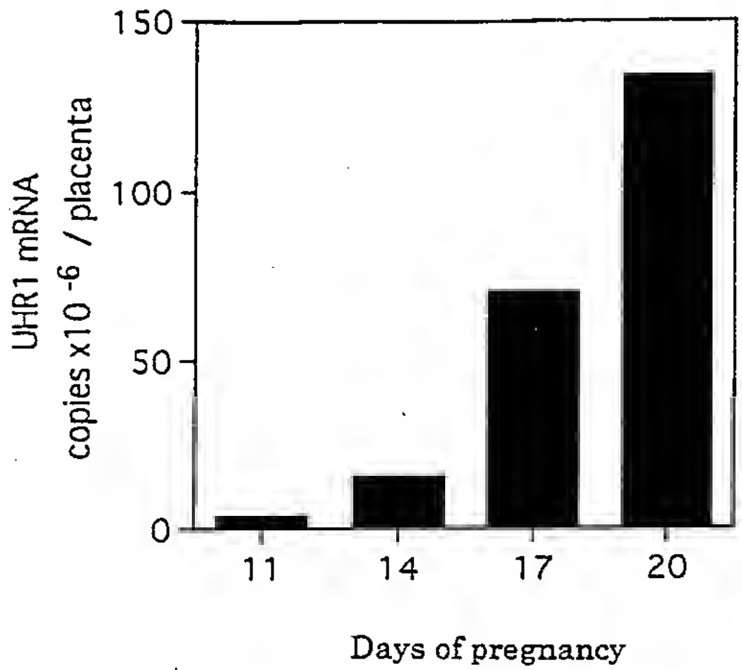
Cell Culture:Rat Anterior Pituitary
Primary Culture
(from F344/N Female Lactating)
5.0×10^{5}/well,
for 4 Days (n=4)
(Poly-D-Lys. coated 24 well-plates)

Wash 3 times
Pre-Incubation (for 1 hr)
Wash twice, Add Samples
Incubation (for 1 hr)
Sup. Collected, Centrifuged

Assay: Rat [1251] Prolactin
Assay System (RIA) (Amersham)

** : $p<0.01$ (students' t-test, compared to control)
* : $p<0.05$ (students' t-test, compared to control)

Fig. 57


150
100
50
0
UHR1 mRNA
copies x10 -6 / placenta
11
14
17
20
Days of pregnancy

09/446543

Fig. 58

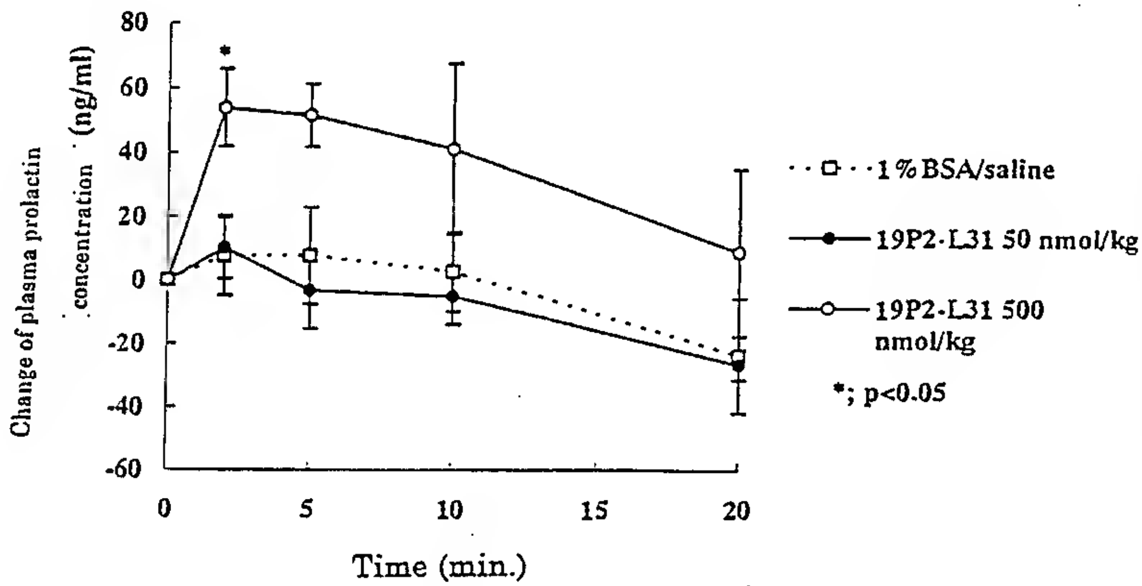


Fig. 59

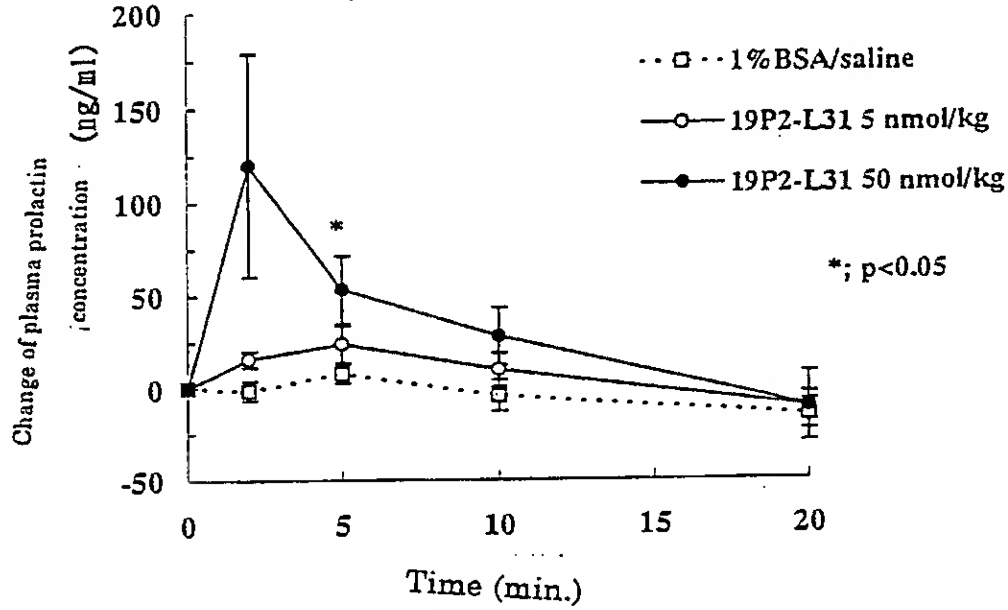
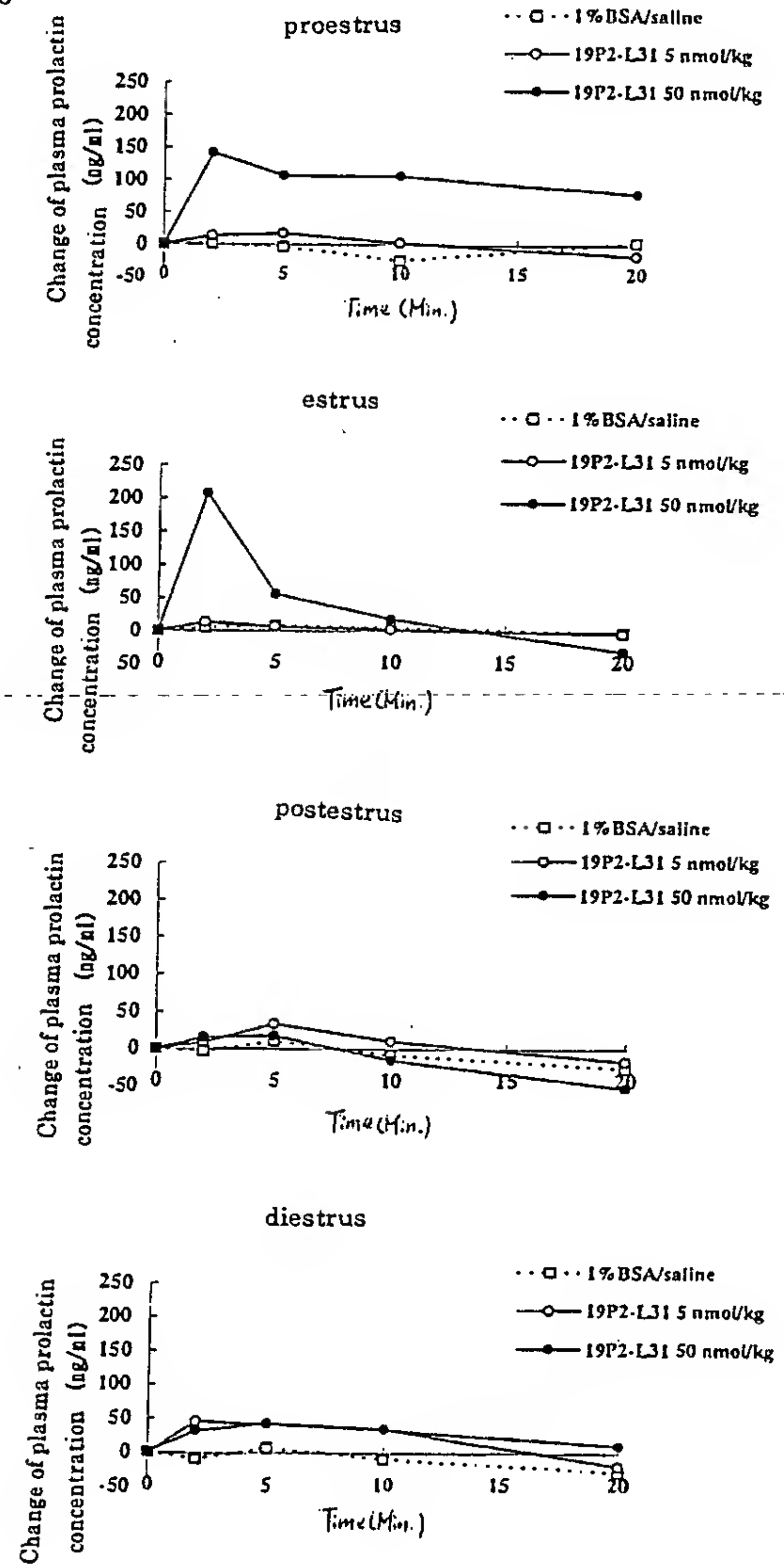

200
150
100
50
0
-50
Change of plasma prolactin concentration (ng/ml)
0
5
10
15
20
Time (min.)
1%BSA/saline
19P2-L31 5 nmol/kg
19P2-L31 50 nmol/kg
*; p<0.05
*

Fig. 60


proestrus
1%BSA/saline
19P2-L31 5 nmol/kg
19P2-L31 50 nmol/kg
Change of plasma prolactin concentration (ng/ml)
Time (Min.)
estrus
1%BSA/saline
19P2-L31 5 nmol/kg
19P2-L31 50 nmol/kg
Change of plasma prolactin concentration (ng/ml)
Time (Min.)
postestrus
1%BSA/saline
19P2-L31 5 nmol/kg
19P2-L31 50 nmol/kg
Change of plasma prolactin concentration (ng/ml)
Time (Min.)
diestrus
1%BSA/saline
19P2-L31 5 nmol/kg
19P2-L31 50 nmol/kg
Change of plasma prolactin concentration (ng/ml)
Time (Min.)